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Health Checks for People with Down Syndrome: A Pooled Analysis of Three Randomized Controlled Trials

Robert S. Ware [1,2,*], Catherine Franklin [2], Lyn McPherson [1] and Nicholas G. Lennox [2]

[1] School of Medicine and Dentistry, Griffith University, Brisbane 4111, Australia; lyn.mcpherson@griffith.edu.au
[2] Queensland Centre for Intellectual and Developmental Disability, Mater Research Institute-University of Queensland, Brisbane 4101, Australia; c.franklin1@uq.edu.au (C.F.); n.lennox@uq.edu.au (N.G.L.)
* Correspondence: r.ware@griffith.edu.au; Tel.: +61-(0)7-3735-9263

Abstract: Health checks have beneficial effects on health outcomes in adults with intellectual disability; however, little is known about their effect on people with Down syndrome. The aim of this study was to assess the effect of receiving a health check on the unmet health needs of people with Down syndrome. A pooled analysis of three randomized trials conducted by the same Australian research team was undertaken. The trials used the same tools but differed by participant source (adults in 24 h supported accommodation, adults in private dwellings, adolescents living with parents). The intervention was a one-off health check, and the comparator was usual care. Among 216 participants, health actions were more likely to occur for those allocated to receive health checks, including increased hearing (odds ratio = 4.4; 95% confidence interval: 1.2, 16.4), vision (2.7; 1.1, 6.7), and thyroid (2.3; 1.3, 4.2) testing, and weight recording (4.7; 2.5, 8.8). Health checks conducted at the primary-care level produced substantially increased attention to the health needs of people with Down syndrome.

Keywords: Down syndrome; health assessment; health check; health promotion; intellectual disability; preventative medicine; primary healthcare

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1. Introduction

Down syndrome is the most common known aetiology of intellectual disability in developed countries [1,2]. While the incidence of Down syndrome varies from country to country, in Australia, it was recently estimated to be 8.6 per 10,000 births [3]. There has been a dramatic increase in life expectancy in recent decades [4], with a recent study showing one in three Japanese people with Down syndrome living to over 60 years [5]. A consequence of this increase in lifespan is an increased focus on the medical and social needs of people with Down syndrome as they enter middle and older age [6].

People with Down syndrome have syndrome-specific co-morbidity with the most prevalent conditions being obesity, epilepsy, constipation, ataxic/gait disorders, and visual and hearing impairment [7,8]. In a recent retrospective chart review of 151 people with Down syndrome attending a rehabilitation centre, Kanbara and colleagues [9] reported a prevalence of endocrine disorders, particularly obesity, of 70%. The most common cause of death is respiratory infection, in part related to immunodeficiencies [10]. People with Down syndrome have a significantly increased risk of developing mental health conditions compared to the general population [11]. Although there is a lower reported rate of psychiatric disorders than in other individuals with intellectual and developmental disability, there are also different rates and types of concurring psychiatric disorders [12–15]. People with Down syndrome are more likely to be diagnosed with testicular cancer and leukemia [16] relative to their non-disabled peers. Consequently, screening and prevention in people with Down syndrome should not automatically mirror the screening or prevention guidelines of the general population. Recently updated healthcare guidelines for adults with Down

syndrome suggest that there are several health issues that should be checked annually. These include measurements of the person's weight, cardiovascular health and thyroid health, and diabetes blood screening [17], although the guideline's authors concluded that the lack of quality evidence limited their strength.

Rates of conductive hearing loss and visual impairment are increased [18], as this population is at an increased risk of narrow ear canals and associated middle ear infections and eye conditions, including premature cataracts and keratoconus. Health conditions, such as vision and hearing loss, can be more difficult to detect in people with Down syndrome due to communication difficulties [19], while conditions presenting with non-specific physical and mental health problems, such as thyroid disease, can be easily missed and can lead to a myriad of problems if undiagnosed and untreated.

Health checks are the only intervention demonstrated to significantly increase health actions conducive to beneficial health outcomes at the primary-care level in people with intellectual disability [20]. There is some evidence that health checks may be the most beneficial for the prevention of morbidities, but do not improve survival once a person has an existing health condition such as diabetes or cancer [21]. While there is growing evidence that providing health checks for all individuals with intellectual disabilities is good practice [22–24], there are specific health issues that are more common for people with Down syndrome, e.g., obesity, gait disorders, and hearing impairments, that require the adaption of universal health checks [8]. However, in the Welsh study cited above, a health check was found to be associated with overall improved survival for those with Down syndrome [21], but there is no evidence on the specific benefits of a health check for this population.

The Comprehensive Health Assessment Program (CHAP) is a health check that has been successfully trialled among people with intellectual disability across three randomized controlled trials conducted among people with intellectual disability living in the community in Southern Queensland, Australia [23,25,26], and all have shown the benefit of health screening on health promotion and disease prevention activities. Although each of the trials included people with Down syndrome, the reported analysis was not specific to aetiology of intellectual disability. Given the specific health needs of people with Down syndrome, it is important to identify whether health checks can reduce unmet health needs in this population. We have conducted an individual patient data pooled analysis of the three above-mentioned trials. The aim of this study was to evaluate the effects of a health check on health promotion and disease prevention activities among people with Down syndrome living in the community.

2. Materials and Methods

Data were combined from three randomized trials conducted by the same research team in Southern Queensland, Australia. This study has been reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [27]. In all studies, the same health check was used, and outcomes were recorded according to the same criteria. The first trial, known as the Endeavour Foundation CHAP (EF-CHAP), was conducted in 2000–2001 among adults who lived in the community in 24 h supported accommodation [23]. All participants were clients of the same non-governmental support provider and were recruited to the study with the help of the provider. Randomization clusters were groups of participants who shared a residence or primary care physician. The intervention assessed was a health check versus usual care. The second trial, known as the Advocacy and Health (A&H) Study, was conducted in 2004–2005 among participants who resided in private dwellings [25]. Randomization clusters were groups of participants who shared a primary care physician. This trial was designed to test two interventions, a health check and a health diary (a hand-held personal health plan designed for ongoing use in all medical consultations). In this 2 × 2 factorial trial, there was no interaction effect between the health check and health diary, so we have compared health actions among participants allocated to receive the health check against those who were allocated to usual

care, ignoring whether they received a health diary. The third trial, known as the Ask Study, was conducted in 2007–2009 among school-attending adolescents [26]. Adolescents resided in private dwellings under the care of a parent or guardian. Randomization clusters were schools. The intervention assessed was a health package, comprising a health check, health diary, and classroom-based health education, compared with usual care. All trials were designed on an 'encouragement' basis, with participants allocated to receive health checks encouraged to contact their primary care physician to book an appointment with the purpose of conducting the health check [28]. In Australia, people with Down syndrome do not pay a consultation fee for an appointment of this kind, and consequently there was no financial disincentive for individuals allocated to receive a health check to book a primary-care appointment.

At study entry, participants' carers completed a questionnaire regarding the demographic, social, and clinical characteristics of the person with Down syndrome. Participants were identified as having Down syndrome if their carer responded to the question "What is the cause of intellectual disability?" ("What is the cause of the young person's intellectual disability?" in the Ask Study) by marking the check-box adjacent to the option "Down syndrome". Other characteristics recorded included age, gender, and level of disability.

The health check used in all trials was the Comprehensive Health Assessment Program (CHAP). The health check was a single-use booklet. The length of the booklet ranged from 21 (EF-CHAP Study) to 32 (Ask Study) pages. The booklets were developed to be easy to read and attractive [29]. The content of the booklets differed slightly by study, but the format remained consistent. The booklet was organized in two parts. The first part consisted of questions regarding the health history, and current health status, of the person with Down syndrome, and was completed by the person with Down syndrome's carer prior to the primary care consultation. The second part consisted of the health check, which involved a review of the history and a targeted examination conducted by the primary care physician, before the physician and carer completed a health action plan. The booklet contained a list of commonly unrecognized or poorly managed conditions in this population and a chart of syndrome-specific comorbidity, to prompt the physician and inform the carer. After examination, the carer retained a copy of the health plan, while the health check booklet was posted to the research team.

At the completion of each study, evidence of health promotion and disease prevention activities was extracted from primary care medical records. The outcome for each study was the 12-month post-intervention cumulative incidence rate for each outcome under investigation. Outcomes considered were vision and hearing tests undertaken and impairments detected, otoscopies performed, vaccinations including tetanus, hepatitis B, and influenza, and also blood pressure checks, having weight recorded, thyroid tests, and skin examinations. The occurrence of each of these health actions for twelve months post health check (or nominated starting date for participants who did not receive a health check) was recorded. Data extractors were masked to the intervention group. Health check receipt for participants allocated to receive health checks was confirmed by either the return of the health check booklet to the research team or the mention of a health check in the primary care medical records.

The original data sets were combined and participants with Down syndrome were identified. Summary statistics are reported as the median (25th to 75th percentile) for variables measured on an interval scale, and as frequency (percentage) for categorical variables. The association between allocation to a treatment group (health check/usual care) and each health-related outcome was calculated using a multi-level mixed-effects logistic regression model. The treatment group was included as the fixed effect, and the primary care physician and study were included as random effects to account for the possible non-independence of results within physicians and studies, with physician nested within study. Effect estimates are reported as odds ratios and 95% confidence intervals. Data were analysed on an 'intention-to-treat' basis, with individuals allocated to receive a health check analysed in the 'health check' group, regardless of whether they actually

attended the primary care practice to receive the health check. Analyses were conducted using Stata Statistical Software v14.1 (Statacorp, College Station, TX, USA).

3. Results

The three trials enrolled a total of 234 people with Down syndrome, of whom medical records were collected for 215 (92%): 109 were allocated to receive health checks and 106 to usual care. Participant flow through the three included trials is displayed in Figure 1. In the EF-CHAP Study, data were collected for 112 participants (97% of those enrolled), and health check receipt was confirmed for 54/56 allocated to receive them. In the A&H Study, data were collected for 37 participants (86% of those enrolled), and health check receipt was confirmed for 16/17. In the Ask Study, data were collected for 66 participants (87% of those enrolled) and health check receipt was confirmed for 28/36. Participants were predominantly male (57%), and in the trials focusing on adults, they had a median age of 37 years (range: 19 to 79) (Table 1). Key demographic and clinical characteristics were balanced between intervention groups in all three studies. The 12-month cumulative incidence of six health promotion activities is displayed in the lower half of Table 1. The percentage of individuals with Down syndrome who had a recorded vision test in the 12 months before they entered one of the three included trials ranged from 7% to 12%. The most commonly recorded activity was a thyroid test (range: 18% to 39%).

Table 1. Baseline demographic and clinical characteristics of adults with Down syndrome in the intervention and control arms of included studies.

Participant Characteristics	EF-CHAP Study		A&H Study		Ask Study	
	Health Check	No Health Check	Health Check	No Health Check	Health Check	No Health Check
Participants, *n*	57	58	19	24	42	34
Clusters, *n*	12	13	12	16	17	13
Male, *n* (%)	40 (70)	32 (55)	9 (47)	11 (46)	20 (48)	22 (65)
Age (years), median (25th–75th %ile)	38 (31–46)	40 (34–46)	41 (27–55)	34 (27–47)	16 (14–17)	17 (15–18)
Level of disability, *n* (%)	*(N = 55)*	*(N = 56)*	*(N = 11)*	*(N = 21)*		
Mild/Moderate	36 (65)	36 (64)	8 (73)	13 (62)		
Severe/Profound	19 (35)	20 (36)	3 (27)	8 (38)		
Clinical Records, *n* (%)	*(N = 56)*	*(N = 57)*	*(N = 17)*	*(N = 20)*	*(N = 36)*	*(N = 30)*
Vision test	4 (7)	7 (12)	2 (12)	2 (10)	3 (8)	3 (10)
Hearing test	5 (9)	2 (4)	1 (6)	2 (10)	2 (6)	2 (7)
Tetanus booster	23 (41)	21 (37)	7 (41)	4 (20)	0 (0	4 (13)
Hepatitis B booster	20 (36)	16 (28)	4 (24)	4 (20)	2 (6)	1 (3)
Weight recorded	2 (4)	4 (7)	8 (47)	8 (40)	4 (11)	5 (17)
Thyroid test	22 (39)	13 (23)	3 (18)	5 (25)	11 (31)	9 (30)

A&H Study, Advocacy and Health Study; EF-CHAP Study, Endeavour Foundation Comprehensive Health Advocacy Program Study.

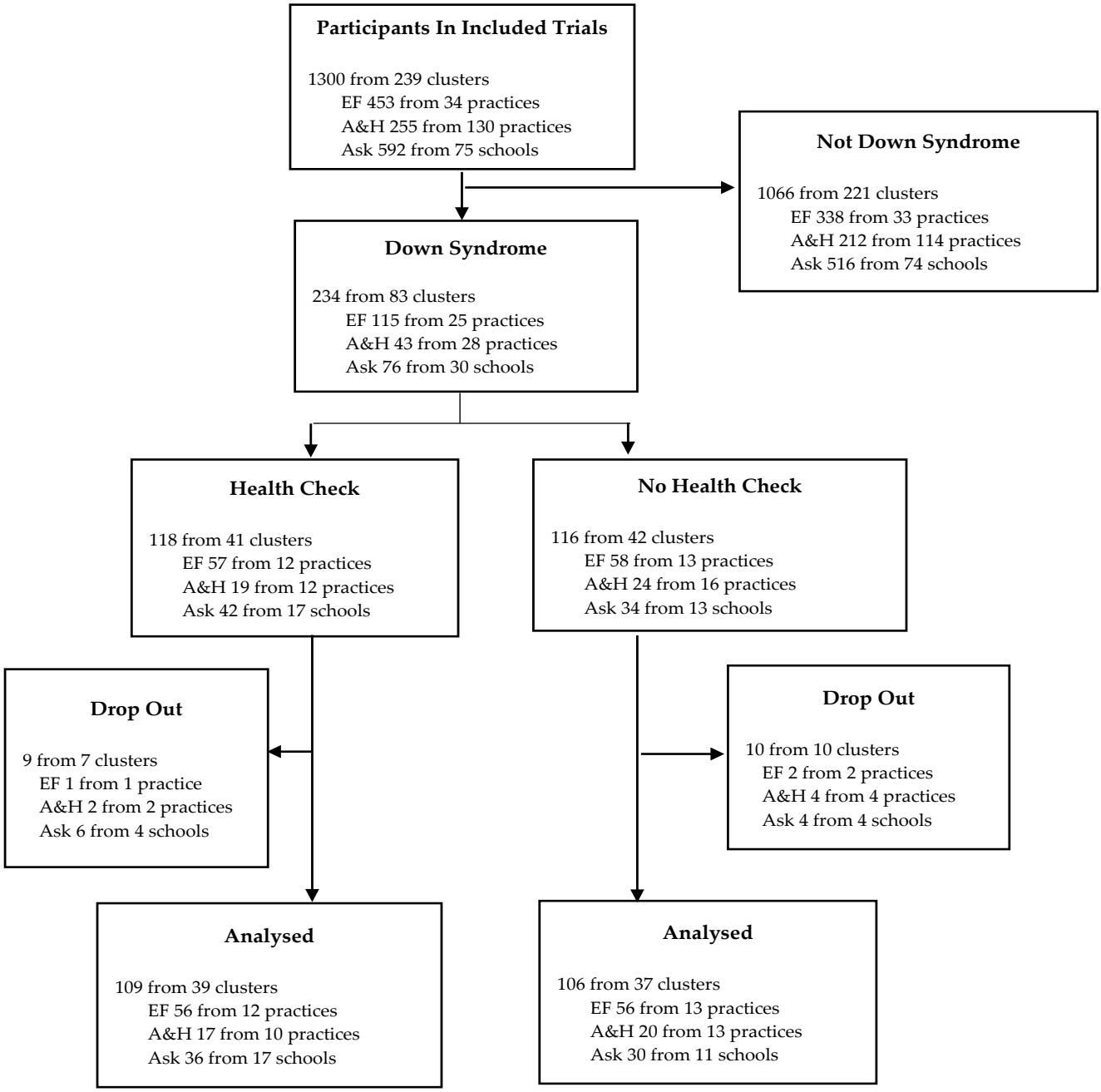

Figure 1. Participant flow through the three included trials.

Table 2 displays post-intervention 12-month cumulative incidence rates, and odds ratios (ORs) with 95% confidence intervals (CIs) for outcomes of interest. In general, participants allocated to receive a health check received far more sensory testing and provision of health promotion and disease prevention activities. In particular, there was an increase in the number of vision (OR = 2.7; 95%CI: 1.1, 6.7) and hearing (4.4; 95%CI: 1.2, 16.4) tests performed, and in the identification of vision impairment (4.4; 95%CI: 1.3, 15.2) and hearing loss. Vaccination rates increased for tetanus/diphtheria (7.7; 95%CI: 2.2, 27.3) and hepatitis B (6.3; 95%CI: 1.4, 29.0). There were also significant increases for weight recorded (4.7; 95%CI: 2.5, 8.8) and thyroid tests (2.3; 95%CI: 1.3, 4.2).

Table 2. Frequency (%) of sensory deficits and health promotion and disease prevention actions, with overall odds ratios and 95% confidence intervals, and odds ratios for each included study.

	Health Check, *n* (%) (*N* = 109)	**No Health Check, *n* (%) (*N* = 107)**	**Odds Ratio (95%CI)**	**Odds Ratio; EF-CHAP Study**	**Odds Ratio; A&H Study**	**Odds Ratio; Ask Study**
Sensory Systems						
Vision test performed	27 (25)	12 (11)	2.7 (1.1, 6.7)	4.3	2.2	2.2
Vision impairment detected	15 (14)	4 (4)	4.4 (1.3, 15.2)	7.4	4.1	3.4
Otoscopic exam	59 (54)	37 (35)	2.3 (1.3, 4.0)	3.1	1.2	2.2
Hearing test	12 (11)	3 (3)	4.4 (1.2, 16.4)	5.4	2.8	n/c
Hearing loss identified	9 (8)	0 (0)	n/c	n/c	n/c	n/c
Vaccinations given						
Tetanus/diphtheria	23 (21)	4 (4)	7.7 (2.2, 27.3)	28.3	7.9	1.8
Hepatitis B	17 (16)	4 (4)	6.3 (1.4, 29.0)	11.4	n/c	1.7
Influenza	55 (50)	41 (39)	2.1 (0.9, 5.0)	2.3	3.4	1.3
Other						
Blood pressure checked	62 (57)	46 (43)	2.2 (0.9, 5.3)	1.9	1.8	3.7
Weight recorded	62 (57)	25 (24)	4.7 (2.5, 8.8)	4.9	3.3	6.2
Skin examination	11 (10)	4 (4)	3.8 (0.8, 17.4)	3.9	4.1	n/c
Thyroid test	47 (43)	26 (24)	2.3 (1.3, 4.2)	3.0	2.9	1.4

A&H Study, Advocacy and Health Study; EF-CHAP Study, Endeavour Foundation Comprehensive Health Advocacy Program Study; n/c, not calculable as no events in one cell.

An examination of the individual odds ratios for each study shows that the effect estimates are consistently in the same direction but vary in magnitude (unsurprisingly given the imprecision due to small study numbers in some cases). For activities that are embedded in day-to-day practice, e.g., blood pressure measurement, or are seasonal, e.g., influenza vaccination, the differences, as would be expected, were less strong. No adverse effects from use of the health check were reported.

4. Discussion

People with Down syndrome who were allocated to receive health checks experienced an increase in clinical activity that is conducive to beneficial health outcomes. In particular, significant increases in the detection of hearing or visual loss, the administration of vaccinations, and recordings of blood pressure and weight were observed. Participants included in this pooled analysis were sourced from a range of settings, including adults residing in paid supported accommodation (EF-CHAP Study), adults living with less formal support, including living independently, living with paid support, or living with families (A&H Study), and adolescents living with their parents (Ask Study). The similarity of effect estimates across the three studies suggests that health checks benefit individuals across all community residential settings.

Use of health checks among adults and adolescents with intellectual disabilities has been previously demonstrated to result in a short-term reduction in deficits in healthcare [24], without leading to increased consultation or medication costs [30]. This study shows that these findings are maintained among the sub-group of people with Down syndrome. An American randomized trial of a population-specific online healthcare tool, the Down Syndrome Clinic to You tool, found that use of the tool increased the number of evaluations indicated with the national Down syndrome healthcare guidelines that were completed or recommended by primary care providers by 1.6 times [31].

Health checks can be beneficial to people with Down syndrome in several different ways. They are an educational tool and reminder for the person with Down syndrome, and also their informal carers and paid support people, to monitor the person's health and remain up to date with preventive healthcare, including vaccinations. This is particularly

important given that people with Down syndrome are most commonly supported informally by family and friends, rather than in state-run disability services [32]. They may also provide guidance to the primary care physician, and prompt them in relation to healthcare issues of increased relevance to people with Down syndrome. A lack of training in primary care is a barrier, as a healthcare provider lacking knowledge and awareness of the needs of people with intellectual disabilities can result in poor communication between the provider and their patient and/or their support person [19].

In the Australian context, as part of the Federal Government's National Roadmap for Improving the Health of People with Intellectual Disability [33], the Department of Health and Aged Care has recently made health checks freely available for all people with intellectual disability, and their future goals include ensuring people with intellectual disability and their supporters are aware of, and can access, annual health checks, and they are working to integrate health checks into primary care software [34].

When compared to the effect of health checks on all people with intellectual disability in the three studies included in the pooled analysis, it can be seen that the magnitude of the effect of health checks on beneficial health actions is greater for people with Down syndrome than it is for people whose intellectual disability is not attributable to a syndrome. This could be due to the 'encouragement' design of the included studies, and the use of 'intention-to-treat' analyses, where individuals randomized to receive health checks are analysed as if they received them. A consequence of this analysis method is that whenever there is non-negligible non-compliance (that is, when people allocated to receive a health check do not attend the primary care practice for the health check to occur), the true effect of health check receipt will be underestimated. Because people with Down syndrome are more likely to complete a health check when offered than people with a non-syndromic intellectual disability are [35], effect estimates from intention-to-treat analyses are more likely to reflect the actual effect of receiving a health check in people with Down syndrome.

Strengths of this individual-patient data pooled analysis include that the data were sourced from three randomized trials with similar data collection and extraction techniques. The members of the research team who extracted data from medical notes were masked to the intervention group. When the effectiveness of masking was investigated in the EF-CHAP Study, masking was compromised in 70% of cases where a health check had been completed, as physicians recorded in their notes that a health check had been performed. A comparative analysis between outcome rates in this group and the remaining 30% found limited evidence of recorder bias. None of the three studies included are likely to be biased due to differential attrition or non-compliance as all studies had excellent follow up and health check receipt was confirmed for 90% of participants allocated to receive health checks. Heterogeneity is unlikely to be a major problem in this analysis, as the three trials were conducted by the same research team, with the only major difference between the studies being the source of participants. Any differences in methods between studies seem unlikely to have caused major bias, given that effect estimates are similar for most measured outcome variables. A limitation may be the age of these data; however, findings are likely to remain accurate as the relationship between health check receipt and healthcare activity is unlikely to have changed significantly since these data were collected. These results are likely to be generalizable to adults with Down syndrome in other high-income countries, as study participants are likely to be representative of the community-dwelling population in such countries, with regards to age, gender, level of intellectual disability, and residential/support arrangements.

This study is the first to use data from randomized controlled trials to quantify the benefit of a primary-care-level health promotion tool on health promotion activities for people with Down syndrome. These findings should inform primary-care choices for people with Down syndrome, their carers, and their physicians. Most of the health outcomes recorded in this study are intermediate steps on the pathway to better health, and we are unable to conclude that adults with Down syndrome will achieve better health over their life course as a result of receiving a health check. However, the significant increase in health

actions following health check receipt suggests that health checks are likely to provide real benefit, which may be magnified by repeated use at regular intervals [36]. Further research into the long-term benefits of health checks is required to determine their sustainability, and to investigate whether they lead to reductions in morbidity and premature mortality. Although periodic health checks for adults with intellectual disability are seen to have merit as a preventative and equitable healthcare tool [37], barriers to their implementation remain, and identifying and developing strategies to overcome these barriers should be a focus of future research.

5. Conclusions

In this pooled analysis of 216 individuals with Down syndrome from three randomized trials, health checks conducted at the primary-care level led to clinically and statistically significantly greater attention to unmet health needs. Health checks are a cost-neutral proactive approach to preventative healthcare. They have the potential to alleviate a large portion of the burden of disease arising from having Down syndrome by contributing to promoting and maintaining good health through increasing awareness of health issues and healthy aging.

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Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki. Each of the three included studies was approved by the Human Research Ethics Committee of The University of Queensland. The details are as follows: Lennox et al., 2007—Ethics approval was granted by the University of Queensland Ethical Review Committee on 27 April 1998 (Project No. B/46/SocPrevMed(DDU)/NHMRC/GPEP/98); Lennox et al., 2010—Ethics approval was granted by the University of Queensland Ethical Review Committee on 20 January 1999 (Project No. B/216/SocPrevMed/99); Lennox et al., 2016—Ethics approval was granted by both the University of Queensland Behavioural and Social Sciences Ethical Review Committee on 31 December 2010 (Clearance No.: 2004000081) and also the Queensland Government Department of Education and the Arts (File No.: 550/27/424).

Informed Consent Statement: Informed consent to participate was obtained from all study participants. In the EF-CHAP and A&H Studies, consent was obtained from the person with Down syndrome and/or their guardian (as appropriate), and their primary care physician. In the Ask Study, consent was additionally obtained from the principal and teachers of the school the adolescent attended.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to patient privacy requirements related to the clinical data.

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Conflicts of Interest: Within Australia, use of the CHAP is free to people with intellectual disability. Outside Australia, UniQuest, a University of Queensland corporate branch, licenses the usage of the CHAP. One-third of the profit is paid to Nicholas G. Lennox (the fourth author). Robert S. Ware, Catherine Franklin, Lyn McPherson, and Nicholas G. Lennox are either currently or have previously been affiliated with the Queensland Centre for Intellectual and Developmental Disability, the University of Queensland, which receives another one-third of the commission to support the centre's research. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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