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Long-term motor outcomes of very preterm and/or very low birth weight individuals without cerebral palsy: A review of the current evidence

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ABSTRACT

We reviewed literature on long-term motor outcomes of individuals aged five years or older born very preterm (VP: ≤32 weeks of gestation) or with very low birth weight (VLBW: ≤1500g), without cerebral palsy (CP). PubMed produced 2827 articles, whereof 38 were eligible. Assessed by standardised and norm-based motor tests, the Movement Assessment Battery for Children being the most widely used, VP/VLBW individuals showed poorer motor skills compared with term-born controls with differences of approximately 1 SD in magnitude. Some studies assessed subdomains and differences were present in fine motor/manual dexterity, ball skills and gross motor/balance. Prevalence of motor problems varied largely from 8-37% in studies with cut-off at the 5th percentile or −1.5 SD to 12–71% in studies with cut-off at the 15th percentile or −1 SD. This review shows that the degree of motor impairments continues to be substantial among VP/VLBW individuals who do not develop CP.

1. Introduction

Motor function is one of the very early signs of typical or adverse neurodevelopment in the child's first year of life [1]. Motor impairments that might be seen in children born preterm vary from cerebral palsy (CP) to minor or subtle motor problems. Most children do not develop CP [2], and minor motor problems might not be evident before early school age when being competent in various motor skills becomes increasingly important for everyday life activities [2]. Fine motor skills or manual dexterity are required for writing, typing, drawing and manipulating objects, while gross motor or balance skills are required amongst others for walking, running and jumping. Further, ball skills include both fine and gross motor skills, and are important for many sports and leisure activities as the child grows older.

Motor problems have been consistently reported in children born very preterm (VP: ≤32 weeks) and/or with very low birth weight (VLBW: ≤1500 g). Over the past decades, there has been increased survival of VP/VLBW children, due to advances in prenatal and newborn care. However, rates of adverse neurodevelopmental outcomes have been relatively stable, with a slight decrease in moderate to severe CP [3–5] and an increase in non-CP motor impairment among extremely preterm (EP: ≤28 weeks) and/or extremely low birth weight (ELBW: ≤1000g) [6,7].

Motor problems, or developmental coordination disorder (DCD) as used by some authors, are usually defined as a score below a cut-off on a standardised motor test, compared with a normative sample or a control group. There are different recommendations as to cut-offs, ranging from scores −2 SD or < 5th percentile [8] to −1 SD or < 15th percentile [9].

Three systematic reviews on motor outcomes of VP/VLBW survivors

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have been published previously [10–12], and in addition, five reviews including any children born preterm or with low birth weight (< 37 weeks/ < 2500 g) [13–17]. De Kieviet et al., 2009 [11] investigated the relationship between VP/VLBW and motor development from birth through adolescence. In comparison with term-born peers, VP/VLBW children obtained significantly lower scores on all the three motor tests included: the Bayley Scales of Infant Development version II, the Movement Assessment Battery for Children (Movement ABC) and the Bruininks-Oseretsky Test of Motor Proficiency (BOTMP). Edwards et al., 2011 [10] concluded that DCD was more prevalent in the VP/VLBW population than full-term/normal birth weight children, with significantly greater odds of developing the disorder (6.29; 95%CI: 4.37–9.05 for scoring < 5th percentile and 8.66; 95%CI: 3.40–22.07 for scoring 5 to 15th percentile). Both reviews included several studies that did not exclude children with mild CP. FitzGerald et al., 2018 [12] concluded that VP children aged 3–6 years had poorer motor outcomes compared with term-born children using the International Classification of Functioning, Disability and Health domains of body structure and function and activity.

We aimed to review long-term motor outcomes including domain-specific motor skills, assessed by standardised motor tests, of VP/VLBW children with no manifest CP compared with term-born controls. We also examined the prevalence of motor problems in VP/VLBW children and risk factors for these problems. We focused on individuals ≥5 years of age, which is a commonly used cut-off in health statistics and the age when hospital follow-up programmes generally are terminated.

2. Methods

A comprehensive literature search was carried out by one author (PH) in MEDLINE Database, using PubMed, between 8 October and 6 November 2019. The search produced 2827 articles (Fig. 1). Search terms are listed in Appendix A.

One author (KAIE) conducted the initial screening of titles and abstracts, using the following inclusion criteria: exposure was VP/VLBW (gestational age ≤32 weeks or birth weight ≤1500g), age of assessment ≥5 years, motor outcome was assessed by a standardised and norm-based motor test, the results were reported as continuous scores (mean/median) compared with a control group or as proportion of children with motor problems according to a defined cut-off. The studies had to be observational cohort studies, exclude participants with all degrees of CP or present results for participants without CP. No study population size or publication year restrictions were applied. Included studies had to be original research articles with full-text available in English. If more than one study reported the same findings on the same cohort assessed at the same age only the publication on the original or larger study sample was included in the review.

Two authors (KAIE and TU) assessed the 230 remaining articles for eligibility, checking the full-texts against the above criteria, resulting in 38 original articles for the final review (Fig. 1). Key characteristics and outcomes were extracted and entered into Tables 1 and 2 by four authors (KAIE, TU, MT and PH). A qualitative synthesis of the included studies was performed.

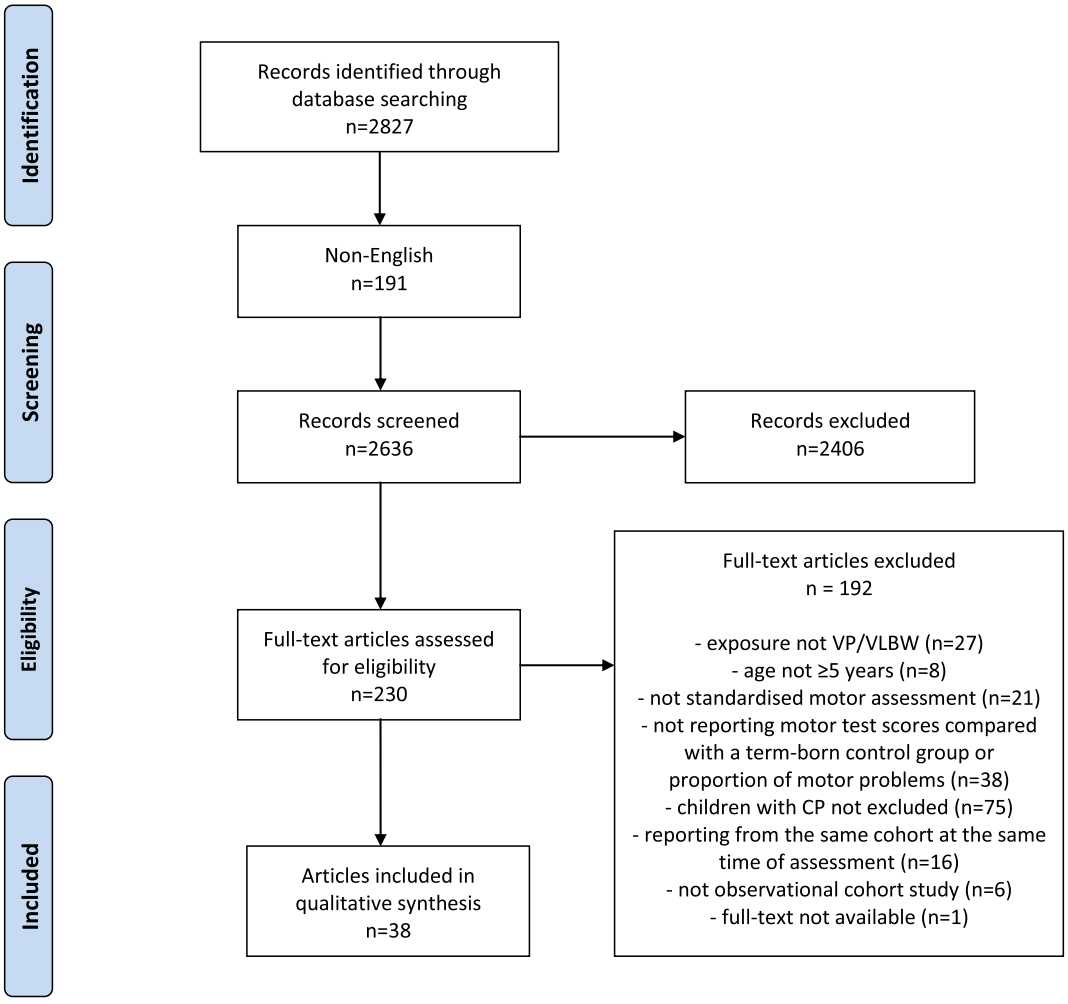

Fig. 1. Flow of article selection for review. CP: Cerebral palsy; VLBW: Very low birth weight; VP: Very preterm.

Table 1
Characteristics of included articles in the order of years of birth of the study participants.

Citation	Setting	Design (n)	BW/GA criteria	Exclusions	Term control group	Birth year	Mean age	Motor outcome	Continuous motor test scores[a]	Cut-off for motor problems	Risk factors[b]
Klein et al., 1989 [42]	USA	Hospital-based cohort (n = 65)	≤1500g	CP, congenital cataracts, fetal alcohol syndrome, mental retardation	Yes	1976	9.3 y	Purdue Pegboard	Mean (SD)	No	Yes
Saigal et al., 1991 [41]	Canada	Regional cohort (n = 68)	< 1000g	CP, hydrocephalus, IQ < 85, blindness, deafness	Yes	1977–1981	7.8 y	BOTMP	Mean (SD)	No	No
Marlow et al., 1989 [38]	England	Hospital-based cohort (n = 53)	< 1251g	CP	Yes	1980–1981	6.1 y	TOMI	Median (IQR)	No	Yes[c]
Marlow et al., 1993 [37]	England	Hospital-based cohort (n = 51)	< 1251g	CP	Yes	1980–1981	8.0 y	TOMI	Median (IQR)	No	No
Powls et al., 1995 [35]	England	Hospital-based cohort (n = 47)	< 1251g	Major neuro-developmental impairment (no CP reported by Marlow et al. [37, 38])	Yes	1980–1981	12-13 y	Movement ABC	Median (IQR)	< 5th percentile; < 15th percentile	Yes
Holsti et al., 2002 [59]	Canada	Regional cohort (n = 73)	≤800g	Neurosensory handicaps, ambulatory CP, verbal and performance IQ < 85	Yes	1982–1987	8.8 y	BOTMP	No[d]	< -2SD[e]; < -1.5SD; < -1SD	Yes
Weindrich et al., 2003 [21]	Germany	Regional cohort (n = 29)	< 1500g	CP, severe learning disability, blindness	Yes	1986–1988	10.9 y	KTK	Mean (SE)[f]	No	No
Evensen et al., 2009 [39]	Norway	Regional cohort (n = 51)	≤1500g	CP, congenital anomalies, syndromes	Yes	1986–1988	14.2 y	Movement ABC	Median (IQR)	< 5th percentile; < 15th percentile	No
Husby et al., 2013 [31]	Norway	Regional cohort, subsample (n = 36)	≤1500g	Congenital anomalies, syndromes. Results presented for adults without CP (n = 32)	Yes	1986–1988	22.5 y	Movement ABC-2; HiMAT; GP	Mean (SD)	No[g]	No
Wocadlo & Rieger 2008 [60]	Australia	Hospital-based cohort (n = 323)	< 30 wks	CP, IQ < 76, blindness, hearing impairment	No	1987–1997	8 y	BOTMP	No	≤5th percentile; < 15th percentile	Yes
Keller et al., 1998 [22]	Canada	Regional cohort, subsample (n = 34)	< 1500g; < 1000g	Neuromuscular disability	Yes	1988–1990	6.4 y	KTK	Mean (SD)	No	No
Short el al. 2003 [40]	USA	Regional cohort (n = 173)	< 1500g	Results presented for children without neurological problems (n = 104)	Yes	1989–1991	8 y	BOTMP Short Form	Mean (SD)	No	Yes
Davis et al., 2007 [33]	Australia	Regional cohort (n = 255)	< 1000g/ < 28 wks	CP, IQ < −2SD	Yes	1991–1992	8.7 y	Movement ABC	Median (IQR)	< 5th percentile; < 15th percentile	Yes[c]
Torrioli et al., 2000 [29]	Italy	Hospital-based cohort (n = 36)	< 1500g	CP, mental retardation, blindness, deafness, born with specific diseases	Yes	1991–1993	4.9 y	Movement ABC	Mean (SD)	≤15th percentile	Yes
Rademaker et al., 2004 [36]	The Netherlands	Regional cohort (n = 204)	≤1500g/≤32 wks	Congenital abnormalities, chromosomal disorders. Results presented for children without CP (n = 189)	Yes	1991–1993	7-8y	Movement ABC	Median (range)	< 5th percentile; ≤15th percentile	No
Seitz et al., 2006 [61]	Switzerland	Hospital-based[h] cohort (n = 74)	< 1250g	CP, IQ < 70	No	1992–1994	6.0 y	ZNA	No	< 10th percentile	No
Natalucci et al., 2013 [62]	Switzerland	Hospital-based[h] cohort (n = 65)	< 1250g	CP, mental retardation, severe behavioural problems	No	1992–1994	10.3 y	ZNA	No	< 10th percentile	No
Feder et al., 2005 [44]	Canada	Regional cohort (n = 42)	< 1250g/ < 34 wks	CP, cognitive impairment, chromosomal abnormalities, genetic syndromes, visual or hearing impairment, IVH grade 3	Yes	1992–1994	6.6 y	BOTMP subtests	Mean (SD)	No	No
Zanudin et al., 2012 [57]	Australia	Hospital-based cohort (n = 48)	< 1000g	CP, general cognitive ability < -2SD at 4 y	No	1992–1994	12.4 y	Movement ABC	No	≤15th percentile	Yes[c]

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Table 1 (*continued*)

Citation	Setting	Design (n)	BW/GA criteria	Exclusions	Term control group	Birth year	Mean age	Motor outcome	Continuous motor test scores[a]	Cut-off for motor problems	Risk factors[b]
Hack et al., 2005 [58]	USA	Hospital-based[h] cohort (n = 219)	< 1000g	Results presented for children without CP, deafness or blindness (n = 183)	Yes	1992–1995	8 y	BOTMP Short Form	No	< -2SD; < -1SD	No
Goyen & Lui 2009 [34]	Australia	Hospital-based[h] cohort (n = 50)	< 1000g/ < 29 wks	CP, IQ < 85, visual or hearing impairment	Yes	1992–1995	8.8 y	Movement ABC	Median (IQR)	< -1.5SD (5th percentile); < -1SD (15th percentile)	Yes[c]
Esbjørn et al., 2006 [28]	Denmark	National cohort (n = 207)	< 1000g/ < 28 wks	Results presented for children without CP or visual impairments (n = 190)	Yes	1994–1995	5.1 y	Movement ABC	Mean (SD); adjusted mean (SEM)[i]	No	No
Marlow et al., 2007 [43]	UK and Ireland	National cohort (n = 180)	≤25 wks	CP or hypotonia resulting in reduced mobility	Yes	1995	6.3 y	Movement ABC subtests	Median (IQR)	No	Yes
Dewey et al., 2011 [55]	Canada	Regional cohort (n = 103)	≤1000g	CP, IQ < 70, visual impairment	No	Not reported (assessed 2001–2005)	5 y	Movement ABC	No	≤15th percentile	Yes[c]
Janssen et al., 2009 [56]	The Netherlands	Hospital-based cohort (n = 371)	≤32 wks	CP, chromosomal disorders, neuromuscular diseases	No	1996–2001	5.3 y	Movement ABC	No	< 15th percentile	Yes[c]
Spittle et al., 2018 [6]	Australia	Regional cohort (n = 189; 191)	< 1000g/ < 28 wks	Results presented for children without CP (n = 168; 169)	Yes	1997; 2005	8 y	Movement ABC; MovementABC-2	No	< 5th percentile; ≤5th percentile	Yes[c]
Leversen et al., 2011 [45]	Norway	National cohort (n = 306)	< 1000g/ < 28 wks	Results presented for children without CP, blindness, deafness or autism (n = 261)	No	1999–2000	5.8 y	Movement ABC	No	< 5th percentile	Yes[c]
Grunewaldt et al., 2014 [32]	Norway	Regional cohort (n = 31)	< 1000g	Congenital syndromes. Results presented for children without CP (n = 23)	Yes	1999–2001	10.2 y	MovementABC-2	Mean (95% CI)	No	No
Tanis et al., 2012 [46]	The Netherlands	Hospital-based cohort (n = 56)	< 32 wks, SGA and AGA	Chromosomal and congenital abnormalities, none had CP	No (VP AGA as control)	2000–2001	8.6 y	Movement ABC	No	< 5th percentile; ≤15th percentile	Yes
Flamand et al., 2012 [47]	Canada	Hospital-based cohort, subsample (n = 10)	≤32 wks	CP, stroke, sensory impairment, small size for GA, IQ < 70, medication for ADHD, twins, neonatal complications	Yes	Not reported	8.5 y	Movement ABC	Mean (SD) percentile	≤5th percentile; ≤15th percentile	Yes
Zwicker et al., 2013 [48]	Canada	Hospital-based cohort (n = 157)	< 1250g	CP, IQ < 70, blindness	No	Not reported (assessed 2005–2009)	4.5 y-5.9 y	Movement ABC	No	≤5th percentile; ≤15th percentile	Yes[c]
Oliveira et al., 2011 [30]	Brazil	Regional cohort (n = 23)	≤1500g	Neurological and orthopedic problems, malformations, syndromes, sensory deficits or other disabilities	Yes	2001–2002	5.8 y	Movement ABC	Mean (SD)	< 5th percentile; < 15th percentile	Yes
Spittle et al., 2011 [49]	Australia	Hospital-based cohort (n = 193)	< 1250g/ < 30 wks	Genetic or congenital abnormalities. Results presented for children without CP (n = 178)	No	2001–2003	5 y	Movement ABC	No	≤5th percentile; ≤15th percentile	Yes
Setänen et al., 2016 [50]	Finland	Regional cohort (n = 98)	≤1500g/ < 32 wks	Results presented for children without CP (n = 90)	No	2001–2004	11.2 y	MovementABC-2	No	≤5th percentile; ≤15th percentile	Yes
Kurpershoek et al., 2016 [51]	The Netherlands	Hospital-based cohort (n = 94)	< 1000g/ < 30 wks	Severe handicaps, genetic syndrome. Results presented for children without CP (n = 76)	No	Not reported (assessed 2007–2009)	5 y	MovementABC/ ABC-2	No	≤5th percentile; ≤15th percentile	No
Moreira et al., 2014 [54]	Brazil	Hospital-based cohort (n = 100)	< 1500g/ < 35 wks	Abnormal neurological conditions	No	2002–2004	9.4 y	MovementABC-2	No	< 15th percentile	Yes[c]

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Table 1 (*continued*)

Citation	Setting	Design (n)	BW/GA criteria	Exclusions	Term control group	Birth year	Mean age	Motor outcome	Continuous motor test scores[a]	Cut-off for motor problems	Risk factors[b]
Janssen et al., 2016 [53]	The Netherlands	Hospital-based cohort (n = 201)	< 32 wks	CP, blindness, deafness, syndromes	No	2003–2005	5.3 y	MovementABC-2	No	< -2SD[e]; < -1SD	Yes
Bolk et al., 2018 [52]	Sweden	National cohort (n = 229)	< 27 wks	CP, cognitive impairment < -2SD, visual or hearing impairment	Yes	2004–2007	6.5 y	MovementABC-2	No	≤5th percentile[j] ≤15th percentile	Yes

ADHD: Attention Deficit Hyperactivity Disorder; AGA: Appropriate for gestational age; BOTMP: Bruininks-Oseretsky Test of Motor Proficiency; BW: Birth weight; CI: Confidence interval; CP: Cerebral palsy; ELBW: Extremely low birth weight; GA: Gestational age; GP: Grooved Pegboard; HiMAT: High-Level Mobility Assessment Tool; IVH: Intraventricular haemorrhage; IQ: Intellectual quotient; IQR: Interquartile range; KTK: Körperkoordinationstest für Kinder; Movement ABC: Movement Assessment Battery for Children; Movement ABC-2: Movement Assessment Battery for Children-Second edition; SD: Standard deviation; SE: Standard error; SEM: Standard error of measurement; SGA: Small for gestational age; TOMI: Test of Motor Impairment; VP: Very preterm; VLBW: Very low birth weight, ZNA: Zurich Neuromotor Assessment.

[a] Compared with term-born controls.

[b] Modifiers of the association between VP/VLBW and motor outcome, such as other perinatal risk factors, parental factors or sex differences.

[c] Multivariate or multiple regression analyses (only significant variables in the final model reported in this manuscript).

[d] Continuous motor scores not reported for the total ELBW group.

[e] < -2SD not shown in Fig. 2.

[f] Adjusted for sex and psychosocial risk.

[g] Proportion of motor problems not reported for VLBW adults without CP.

[h] Tertiary centre.

[i] Adjusted for age and parental education.

[j] Odds ratio adjusted for mother's education, mother's country of birth, complex sample analysis to adjust for clustering effects caused by presence of twins.

3. Results

3.1. Characteristics of included articles

Table 1 shows characteristics of the included articles, published between 1989 and 2018. Birth year of participants ranged from 1976 to 2007 and mean age at assessment was 5–22.5 years. Twenty-four articles reported outcomes for VP/VLBW and 14 for EP/ELBW children. Included articles were from high-income countries in Europe (n = 20), Australia (n = 6), Canada (n = 7), USA (n = 3) and a middle-income country (Brazil; n = 2) and used the following motor tests: the Movement ABC [18] (n = 18), the Movement Assessment Battery for Children-Second edition [8] (Movement ABC-2) (n = 7), the BOTMP [19] (n = 6), the Test of Motor Impairment (TOMI) [20] (n = 2) (the precursor of Movement ABC), the Körperkoordinationstest für Kinder (KTK) [21,22] (n = 2), the Zurich Neuromotor Assessment (ZNA) [23,24] (n = 2), the High-Level Mobility Assessment Tool (HiMAT) [25] (n = 1), the Grooved Pegboard (n = 1) [26] or the Purdue Pegboard [27] (n = 1) (Appendix B. Table 1).

3.2. Total motor test scores of VP/VLBW individuals without CP compared with term-born controls

Eighteen articles reported continuous total test scores compared with a term-born control group (Table 2). In studies with more than 20 participants, the VP/VLBW children had mean Movement ABC scores 4.0 to 8.5 points lower compared with controls at 5–6 years of age [28–30], corresponding to differences ranging from 0.93 [28] to 1.84 SD [29]. Mean Movement ABC-2 scores were 6.1 [31] to 13.3 [32] points lower, corresponding to a 0.70 SD difference in young adults [31]. The difference in median TOMI, Movement ABC or Movement ABC-2 scores ranged from 1.5 to 7.5 points in children aged 6–14 years [33–39]. Assessed by the BOTMP, mean differences were 10.7 and 4.9 points in VLBW children with and without BPD [40], and 8.0 points in ELBW children [41], corresponding to 0.41 to 0.89 SD difference from their respective control groups at 8 years of age. Measured by the KTK, differences in mean scores between VLBW and control groups ranged from 3 [22] to 7 points [21] and was as large as 12 points (1.50 SD) in ELBW children compared with controls at 6 years [22]. The only adult study [31] reported a difference of 3 points (0.88 SD) between the VLBW and the control group at 22.5 years of age, assessed by the HiMAT. VLBW adults used 5.6–6.3 s more than controls to complete the GP with the non-dominant and dominant hand, a difference of 0.53 and 0.66 SD, respectively [30], similar to the 0.50 SD difference in performance on the Purdue Pegboard in 9-year-old children for all three conditions [42] (Table 2).

3.3. Domain-specific test scores of VP/VLBW individuals without CP compared with term-born controls

Eleven articles reported continuous test scores for subdomains of manual dexterity/fine motor function, ball skills and balance/gross motor function (data not shown). Mean manual dexterity scores on Movement ABC were 1.9 points lower [30], and on Movement ABC-2 2.1 [31] to 7.7 [32] points lower, in VP/VLBW individuals compared with controls, corresponding to differences of 0.39 [31] to 0.91 SD [30]. Differences in median TOMI or Movement ABC manual dexterity scores ranged from 0.5 to 2.0 points [33,34,37–39], and was 1.5 points lower for posting coins in ELBW children [43]. VLBW children had BOTMP scores 1.3 to 5.2 points lower for fine motor and upper limb tasks, and differences ranged from 0.34 to 0.63 SD for the various subtests [44].

For ball skills, VP/VLBW individuals had Movement ABC scores 1.5 points lower [30], and Movement ABC-2 scores 1.1 [32] to 1.4 [31] points lower compared with controls, corresponding to differences of 0.30 [31] to 1.66 SD [30]. The difference in median TOMI and

Table 2
Total motor test scores of VP/VLBW individuals without CP compared with controls as reported in the included articles.

Citation	VP/VLBW n (% male)	Control n (% male)	VP/VLBW	Control	p-value	Difference in mean/ median	Difference in SD units[a]
			Movement ABC[b]; mean (SD/SEM)				
Torrioli et al., 2000 [29]	n = 36 (42%)	Not reported (matched)	15.58 (7.96)	7.08 (4.61)	p < 0.001	8.5	1.84
Esbjørn et al., 2006 [28]	n = 190 (49% of original sample, n = 269)	n = 76 (46%)	10.5 (7.8) 10.7 (SEM 0.6)[c]	6.5 (4.3) 5.5 (SEM 1.1)[c]	p < 0.001 p < 0.001	4.0 5.2	0.93 1.21
Flamand et al., 2012 [47]	n = 10 (60%)	n = 7 (57%)	32.7th (26.5) percentile	60.6th (19.8) percentile	p = 0.038	27.9	1.41
Oliveira et al., 2011 [30]	n = 23 (39%)	n = 23 (not reported)	8.17 (7.10)	3.06 (3.80)	p = 0.002	5.1	1.34
			Movement ABC-2[b]; mean (SD/95% CI)				
Husby et al., 2013 [31]	n = 32 (38%)	n = 37 (41%)	74.1 (14.4)	80.2 (8.7)	p = 0.061	6.1	0.70
Grunewaldt et al., 2014 [32]	n = 23 (35%)	n = 33(49%)	63.8 (55.8–71.8)	77.1 (70.6–83.6)	p = 0.019	13.3	
			TOMI/Movement ABC/Movement ABC-2[b]; median (IQR)				
Marlow et al., 1989 [38]	n = 53 (62%)	n = 53 (62%)	6.0 (4.0–8.75)	3.0 (1.5–4.5)	p < 0.001	3.0	
Marlow et al., 1993 [37]	n = 51 (63%)	n = 59 (not reported)	3.5 (3–5)	2.0 (1–4)	p = 0.0002	1.5	
Powls et al., 1995 [35]	n = 47 (not reported)	n = 60 (not reported)	10 (3.5–16)	2.5 (0.5–6)	p < 0.0001	7.5	
Evensen et al., 2009 [39]	n = 51 (55%)	n = 75 (43%)	10.0 (5.0–14.0)	6.5 (3.0–9.0)	p < 0.001	3.5	
Davis et al., 2007 [33]	n = 255 (46%)	n = 208 (not reported)	4.5 (2.0–10.5)	1.5 (0.5–3.5)	p < 0.001	3.0	
Rademaker et al., 2004 [36]	n = 189 (57%)	n = 21 (62%)	5.5 (range 0–36.5)	2.0 (range 0–10)	Not reported	3.5	
Goyen & Lui 2009 [34]	n = 50 (50%)	Not reported (matched)	8.75 (5–13.6)	5 (2.9–9.7)	p < 0.001	3.75	
			BOTMP[b]; mean (SD)				
Saigal et al., 1991 [41]	n = 68 (44%)	n = 114 (47%)	46.6 (8.9)	54.6 (9.4)	p < 0.0001	8.0	0.85
Short el al. 2003 [40]	BPD n = 49 (45%) VLBW n = 55 (40%)	n = 99 (49%)	BPD 47.1 (13) VLBW 52.9 (12)	57.8 (12)	p = 0.001 for both groups vs. Control	10.7 4.9	0.89 0.41
			KTK[b]; mean (SD)				
Weindrich et al., 2003 [21]	n = 29 (38%)	n = 112 (49%)	98.4 (SE 2.6)[d]	105.4 (SE 1.3)[d]	p < 0.05	7.0	
Keller et al., 1998 [22]	ELBW n = 14 (21%) VLBW n = 20 (75%)	n = 24 (63%)	ELBW 73 (10) VLBW 82 (11)	85 (8)	p < 0.05 for ELBW vs. VLBW and Control	12.0 3.0	1.50 0.38
			HiMAT[b]; mean (SD)				
Husby et al., 2013 [31]	n = 32 (38%)	n = 37 (41%)	46.6 (5.4)	49.6 (3.4)	p = 0.023	3.0	0.88
			GP[b]; mean (SD)				
Husby et al., 2013 [31]	n = 32 (38%)	n = 37 (41%)	Dominant hand 68.5 (16.9) Non-dominant hand 73.9 (13.4)	62.2 (9.5) 68.3 (10.6)	p = 0.064 p = 0.061	6.3 5.6	0.66 0.53
			Purdue Pegboard[b]; mean (SD)				
Klein et al., 1989 [42]	n = 65 (62%)	n = 65 (62%)	Combined hands 8 (2) Right hand 11 (2) Left hand 10 (2)	9 (2) 12 (2) 11 (2)	p < 0.007 < 0.05 < 0.025	1.0 1.0 1.0	0.50 0.50 0.50

BOTMP: Bruininks-Oseretsky Test of Motor Proficiency; BPD: Bronchopulmonal dysplasia; CI: Confidence interval; CP: Cerebral palsy; ELBW: Extremely low birth weight; GP: Grooved Pegboard; HiMAT: High-Level Mobility Assessment Tool; IQR: Interquartile range; KTK: Körperkoordinationstest für Kinder; Movement ABC: Movement Assessment Battery for Children; Movement ABC-2: Movement Assessment Battery for Children-Second edition; SD: Standard deviation; SE: Standard error; SEM: Standard error of measurement; TOMI: Test of Motor Impairment; VP: Very preterm; VLBW: Very low birth weight.

[a] Based on SD of control group.

[b] Scoring is shown in Appendix B. Table 1.

[c] Adjusted for age and parental education.

[d] Adjusted for sex and psychosocial risk.

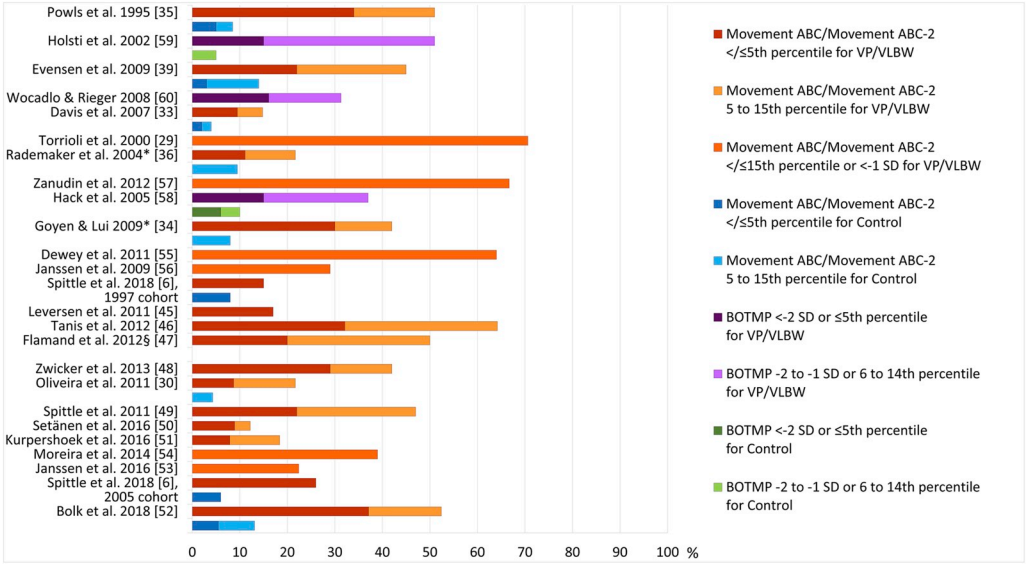

Fig. 2. Prevalence of motor problems in VP/VLBW individuals assessed by using various motor tests and cut-offs in the order of years of birth of the study participants. *No controls < 5th percentile. §No controls ≤5th or 15th percentile. BOTMP: Bruininks-Oseretsky Test of Motor Proficiency; Movement ABC/ABC-2: Movement Assessment Battery for Children/ Second edition; VLBW: Very low birth weight; VP: Very preterm; SD: Standard deviation.

Movement ABC ball skills scores ranged from 0.5 to 1.0 points [33,34,37–39].

In the balance domain, VP/VLBW individuals had Movement ABC-2 scores 2.5 [31] to 5.1 points [32] lower and Movement ABC scores 1.8 points [30] lower than controls, corresponding to a 0.64 [31] to 0.96 SD difference [30]. Differences in median Movement ABC and TOMI balance scores ranged from 0.5 to 2.0 points [33,34,37–39], and were 1.0–2.0 points for heel-toe walking and one-leg balance, respectively [43]. Differences in balance, laterality and jumping task scores of the KTK ranged from 0.50 to 1.00 SD for ELBW children and from 0.13 to 0.62 SD for VLBW children versus controls [22].

3.4. Prevalence of motor problems in VP/VLBW individuals without CP

Prevalence of motor problems among VP/VLBW individuals assessed by the Movement ABC or Movement ABC-2 varied from 7.9 to 37.1% in studies with cut-off at the 5th percentile or −1.5 SD [6,30,33–36,39,45–52], with one third of the studies reporting motor problems in more than a quarter of the children aged 6 to 12–13 years of age (Fig. 2). In studies with cut-off at the 15th percentile or −1 SD, the prevalence ranged from 12.2 to 70.6% [29,30,33–36,39,46–57], with one third of the studies reporting problems in more than half of the children aged 4.9 to 12–13 years of age. Among controls, the prevalence of motor problems in studies using the Movement ABC or Movement ABC-2 varied from 0 to 8.0% (5th percentile) [6,33–36,39,52] and from 0 to 14.0% (15th percentile) [30,33–36,39,47,52]. Using the BOTMP, prevalence of motor problems in VP/VLBW individuals was 15.0–16.1% in studies with cut-off at the 5th percentile or −2 SD [39,58–60] and 31.3–51.0% in studies with cut-off at the 15th percentile or −1 SD [58–60]. The prevalence among controls in studies using the BOTMP varied from 0 to 6.0% (≤5th percentile or < -2 SD) and from 5.0 to 10.0% (< 15th percentile or < -1 SD) [58,59].

3.5. Prevalence of domain-specific problems in VP/VLBW individuals without CP

Manual dexterity problems were present in 3.0% of 5-year-old VP children [53] using a −2 SD cut-off and in 16% of VLBW adolescents [39] using the 5th percentile cut-off on the Movement ABC-2/ABC (data not shown). The prevalence ranged from 21.4% [53] using a −1 SD cut-off to 49% in 9-year-old VLBW children using the 15th centile cut-off [54]. Prevalence of problems in ball skills ranged from 2.5% < -2 SD [53] to 26% < 15th percentile [54], whereas prevalence of balance problems ranged from 3.0% < -2 SD [53] to 35% < 15th percentile [54]. In VLBW adolescents, the odds were significantly increased for having manual dexterity and balance problems < 5th and 15th percentile, but not for problems in ball skills [39]. However, in a Swedish national cohort, not only were the odds of having manual dexterity (adjusted OR: 8.44; 99%CI: 3.64–19.57) and balance problems (OR: 4.24; 99%CI: 1.84–9.72) in 6.5-year-old EP children increased, but the odds were also significantly increased for problems in ball skills (OR: 4.93; 99%CI: 2.26–10.77) [52].

The prevalence of ZNA pure motor scores < 10th percentile was similar (24% and 25%) at 6 [61] and 10 years [62] in the same VLBW cohort. Poor fine motor scores occurred in 38% at 6 years, and 17% at 10 years, while poor gross motor scores occurred in 26% at 6 years and 34% at 10 years. Rates of poor static balance were rather similar at 6 (20%) and 10 years (18%) [62]. Holsti et al., 2002 [59] reported that of the 9-year-old ELBW children that were classified as having DCD based on BOTMP scores < -1 SD on the gross motor, fine motor or battery composite, 57% had a low gross motor composite score, 16% had a low fine motor composite score and 27% had low scores in both gross and fine motor composite areas.

3.6. Risk factors for poor motor outcomes in VP/VLBW individuals without CP

Twenty-five articles reported on risk factors for poor motor outcomes. Several studies found that boys performed worse than girls [33,43,45,48,53,56,57], but one study reported poorer outcome for girls [35] and some found no effect of sex [47,52,59,60].

Apart from sex, lower birth weight [30,48,50,52,54], small for gestational age [29,45,46] or poor fetal growth [6], lower gestational age [45,50,52,53,56] but also increasing gestational age given a birth weight < 1000g [55] were reported as risk factors for motor problems. Among obstetric and maternal risk factors, premature rupture of membranes [34], lower maternal age at childbirth [54], mother being unemployed [54] and poorer family environment resources [30,54] were associated with poorer motor outcome, whereas some reported that mother's education [30,55,56], father's education [30], income [30] or socioeconomic status [55] were not. A long list of neonatal risk factors, such as lower Apgar score after 5 min, neonatal septicaemia and abnormal movements [38], neonatal lung disease [57], retinopathy of prematurity [34,45,52], postnatal corticosteroids [6,40,48,52,55], bronchopulmonal dysplasia (BPD) [40,50,55], and duration on supplemental oxygen [40] and mechanical ventilation [52,60], neonatal surgery [6], white matter abnormalities [49], decreased brain volumes

at term [50], intraventricular haemorrhage (IVH) [6,56] and cystic periventricular leukomalacia (PVL) [6] were reported as risk factors for motor problems in the reviewed articles.

4. Discussion

We identified 38 original publications fulfilling the inclusion criteria. Of them, 23 were not part of the three previous reviews of VP/VLBW children [10–12], as we included more recent publications and articles reporting both continuous motor scores and/or prevalence of motor problems assessed by a wider variety of tests. Age at assessment varied from our lower limit of 5 years and up to 14 years, with the exception of the Norwegian NTNU cohort also assessed at 22.5 years [31]. All studies came from high-income countries except two studies from a middle-income country [30,54].

There were substantial differences between VP/VLBW children and controls across all ages. Typical mean differences in continuous scores were in the order of magnitude of 1 SD. In studies that reported subdomain scores, differences were present across all motor domains, as reported by de Kieviet et al., 2009 [10], with increased risk of poor manual dexterity/fine motor function, ball skills and balance/gross motor function. In accordance with Edwards et al., 2011 [9], the prevalences of motor problems were several-fold larger than those in controls, but with some uncertainty, partly because of low number of cases among term-born controls. There was no evidence that younger children had higher prevalence of motor problems, neither did it seem related to years of birth. Potential reasons for the wide variation in difference in mean scores and prevalence of problems may be related to differences in study designs and settings, selection and exclusion criteria, follow-up rates and applied test norms.

These differences compare with differences in other key outcomes in VP/VLBW children and adults. Cognitive abilities have been extensively studied and remain 0.70 to 0.86 SD lower in VP/VLBW children than in controls [63]. Other examples include pulmonary airflow, showing a similar difference, 0.80 SD, in 1-s forced expiratory flow in VLBW adults [64], whereas the difference in blood pressure is smaller, corresponding to 0.3 SD [65,66]. Together these numbers indicate that poorer motor skills, even without the presence of manifest CP, are an essential part of the "VP/VLBW phenotype" at least in childhood.

There is little evidence on whether and to what extent poorer motor skills persist to adulthood. The only published study extending to adulthood is the Norwegian NTNU cohort [31], which suggests that the deficits in fine and gross motor skills in VLBW children persist to adulthood. While the mean differences with controls were relatively small in comparison with studies in childhood, the proportion of those with motor problems was similar to what was shown in the same cohort at 14 years of age [67]. This paucity of evidence contrasts with the increasing research activity on other outcomes in adult VP/VLBW cohorts and may in part be due to a lack of assessment tools validated for young adults; we argue for incorporating motor outcomes in follow-up studies in these cohorts.

Even though some other reviews have included all degrees of prematurity [13–17], the majority of the included studies focused on VP/VLBW or more immature or smaller subgroups. Much of the improvement in VP/VLBW survival has been related to improvements in resource-intensive neonatal care units in high-resource settings. These typically also have follow-up and medical, social and educational support systems in place, which is reflected in the settings of the included studies. With improving prenatal and newborn care, survival of VP/VLBW infants is increasing also in lower-resource settings [68]. The published results may therefore reflect a conservative estimate in relation to these settings which may also have lower resources for follow-up and support.

According to Spittle & Orton 2014 [69], all forms of motor impairment are associated with comorbidities. Thus, there is reason to believe that the motor problems seen in VP/VLBW children are part of more widespread brain pathology [70], and may act as an early biomarker for cognitive and behavioural problems later in childhood [70]. Motor and coordination problems in childhood and adolescence have been found to be associated with overall psychiatric problems in VLBW adults [71], and elevated levels of inattention and symptoms of anxiety and depression in both ELBW and control adults [72]. These co-occurrent problems may have a greater effect on quality of life, academic achievement and participation in extracurricular activities than the motor impairment itself [69]. Several studies have reported lower physical activity, sports participation and recreational activities among young adults born VP/VLBW [73–77] or less than 34 weeks of gestation [78]. While these differences have usually not been seen in studies measuring physical activity by accelerometry [79], they are accompanied by findings of lower lean body mass [80] and physical fitness [74,81]. They may be a result of a vicious cycle where poor motor coordination have been suggested to play a key role, perhaps together with lower pulmonary airflow [64] and poor visual acuity [39]. This may lead to lower physical self-confidence and perceived physical ability [82], together making physical activity less rewarding, leading to lower degrees of physical activity and may also aggravate the lower exercise capacity and lower lean body mass. Therefore, we believe that promotion of health-enhancing physical activity, with special reference to challenges in motor skills, has potential in improving the health of children and adults born VP/VLBW. Spittle & Orton 2014 [69] argue that a reliable diagnosis of motor impairment requires follow-up into childhood and is important to ensure that the appropriate intervention is implemented. Interventions that are activity-oriented and involve environmental support by family and significant others to facilitate participation across contexts are recommended [9]. However, evidence regarding which interventions are most effective in improving motor outcomes is sparse and few studies have assessed long-term effects [83,84].

Several studies reported neonatal risk and male sex as factors explaining part of the motor problems. These findings are supported by the review of Bos et al., 2013 [17], who reported intrauterine growth restriction, inflammatory conditions and BPD as risk factors for fine motor skill impairments in preterm children. Furthermore, Linsell et al., 2016 [85] reported IVH and/or PVL to be a prominent feature in the medical history of children not only developing CP, but also minor neurological dysfunctions.

This review was based on a systematic literature search. We focused on children aged five years or older, whereas previous reviews also have included younger children. We excluded articles that included even mild degrees of CP, and we present both continuous motor test scores and prevalence of motor problems, as well as domain-specific test scores and problems. One reason for not performing a meta-analysis was the different methods used to assess motor skills. Although most studies used either the Movement ABC or Movement ABC-2, some reported mean (SD), whereas other reported median (IQR or range) scores, and different cut-offs were used to identify motor problems.

4.1. Conclusion

Including recent studies and excluding all degrees of manifest CP, we found that VP/VLBW individuals had poorer motor skills in terms of total test scores, domain-specific test scores and increased prevalence of total motor and domain-specific problems. There was a wide variability in results between studies, however it seemed not related to age or years of birth. The motor problems are present when the children generally no longer attend preterm-specific follow-up programs. Healthcare and education professionals should be aware of increased risk of such problems, to provide appropriate intervention, including environmental adjustments and understanding of their motor problems, to promote participation and reduce the impact on everyday activities and future health problems.

4.2. Practice points

- Children and young adults born very preterm or with very low birth weight have increased risk of poor motor skills in terms of total test scores and domain-specific test scores.
- Healthcare and education professionals should be aware that these problems are manifest when the children generally no longer attend preterm-specific follow-up programs and provide appropriate interventions to reduce the impact on everyday life.

4.3. Research agenda

- Motor problems in the much larger groups of children born moderate and late preterm in high and low resource settings.
- Persistence of motor problems and their significance in later adult life.
- The role of motor problems in developing physical activity habits and consequently physical fitness.
- Interventions and their effectiveness long term.

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Declaration of competing interest

None declared.

Appendix A. Search terms for MEDLINE database using the PubMed search engine

("premature birth"[All Fields] OR "premature infant"[All Fields] OR "born premature"[All Fields] OR "preterm"[All Fields] OR "very preterm"[All Fields] OR "extremely preterm"[All Fields] OR "low birth weight"[All Fields] OR "very low birth weight"[All Fields] OR "extremely low birth weight"[All Fields] OR "Infant, Premature"[All Fields] OR "Infant, Low Birth Weight"[All Fields] OR "Infant, Very Low Birth Weight"[All Fields] OR "Obstetric Labor, Premature"[All Fields] OR "prematurity"[All Fields])

AND

("movement"[All Fields] OR "motor skills"[All Fields] OR "motor function"[All Fields] OR "motor performance"[All Fields] OR "motor impairment"[All Fields] OR "motor delay"[All Fields] OR "motor deficit"[All Fields] OR "motor problems"[All Fields] OR "motor disorders"[All Fields] OR "developmental coordination disorder"[All Fields] OR "DCD"[All Fields] OR "fine motor"[All Fields] OR "gross motor"[All Fields] OR "manual dexterity"[All Fields] OR "hand function"[All Fields] OR "ball skills"[All Fields] OR "balance skill"[All Fields] OR "balance function"[All Fields] OR "static balance"[All Fields] OR "dynamic balance"[All Fields] OR "postural control"[All Fields] OR "postural stability"[All Fields] OR "motor speed"[All Fields] OR "Movement Assessment Battery for Children"[All Fields] OR "Movement ABC"[All Fields] OR "MABC"[All Fields] OR "MABC-2"[All Fields] OR "Bruininks-Oseretsky Test of Motor Proficiency"[All Fields] OR "BOTMP"[All Fields] OR "BOT-2"[All Fields] OR "Motor Skills Disorders"[All Fields])

Appendix. B Table 1. Standardised and norm-based motor tests to describe motor skills and/or identify motor problems in the included articles

Test	Age range	Items included in the test	Scoring
Movement Assessment Battery for Children (Movement ABC) [18]	4-12 y	Eight items in three subscores; manual dexterity (three items), ball skills (two items), static/dynamic balance (three items).	Raw scores converted to standard scores on a 6-point scale (0–5; 0 being optimal score) for each item and summarised to a total impairment score (maximum 40). Scores < 5th and < 15th percentile indicate definite and borderline motor problems.
Movement Assessment Battery for Children-2 Second edition (Movement ABC-2) [8]	3-16 y	Eight items in three subscores; manual dexterity (three items), aiming and catching (two items), balance (three items).	Raw scores converted to standard scores 1–19 for each item (higher indicating better skills) and summarised to a total score (maximum 152). Scores ≤5th and ≤15th percentile denote a significant movement difficulty or suggest the child is at risk of having a movement difficulty.
Test of Motor Impairment (TOMI) [20]	5-12 y	Eight items in three subscores; manual dexterity (three items), ball skills (two items), static and dynamic balance (three items).	Scored on a 3-point scale (0 = no problems, 1 = some problems, 2 = difficulties) and summarised to a total score (maximum 16).
Bruininks-Oseretsky Test of Motor Proficiency (BOTMP) [19]	4.5–14.5 y	Long Form: 46 items in eight subtests; gross motor composite (four subtests), fine motor composite (three subtests) and battery composite (one subtest). Short Form: 14 items from the eight subtests.	Scoring system varies with each item, ranging from a 2-point (pass/fail) to a 16-point scale. Raw scores converted to a numerical point score and composite scores expressed as centile rank, z-score, T score (mean 50; SD 10), stanine or age-equivalent.
Körperkoordinationstest für Kinder (KTK) [21, 22]	5-14 y	Four tasks; walking backward on beams of decreasing width, jumping with each leg separately over an increasing height (number of foam plates), jumping sideways with both feet and moving across the floor by stepping from one plate on a second plate, then relocating the first plate before taking the next step and so on.	Performances converted to a standard score, or motor quotient (MQ). A MQ between 90 and 110 represents normal coordination, while scores < 80 indicate deficiencies in motor ability.
Zurich Neuromotor Assessment (ZNA) [23, 24]	5-18 y	Five components; pure motor tasks, adaptive fine motor, adaptive gross motor, static balance and associated movements.	Raw scores summarised to standard components and expressed as z-scores. Scores < 10th percentile indicate abnormal performance.
High-Level Mobility Assessment Tool (HiMAT) [25]	> 13 y	13 items; walk, walk backwards, walk on toes, walk over obstacle, run, skip, hop forward, bound and walk up/down stairs.	Raw scores are converted to a score on a 5-point scale (0–4), except stair items on a 6-point scale (0–5; higher score indicates better function). Maximal score of 54.

Grooved Pegboard (GP) [26]	> 5 y	Inserting 25 pegs, one at a time, into keyhole-shaped holes with various orientations in a 5 × 5 matrix. Dominant and non-dominant hand are tested.	Raw scores consist of time in seconds to complete the board and number of drops for each hand. Age-specific norms.
Purdue Pegboard [27]]	5-89 y	Placing as many pins as possible in the holes, within a 30 s time period. Preferred hand, non-preferred hand and both hands together are tested.	Raw scores consist of number of pins inserted within the 30 s time period for each hand. Score for the bimanual condition consists of the total number of pairs of pins inserted.

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