

ORIGINAL ARTICLE

Analysis of self-reported activities of daily living, motor performance and physical activity among children and adolescents with cancer: Baseline data from a randomised controlled trial assessed shortly after diagnosis of leukaemia or non-Hodgkin lymphoma

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Abstract

Objective: Cancer diagnosis, treatment side effects and physical inactivity can lead to reduced muscle strength. Patients undergoing acute treatment experience many burdens that can restrict their mobility and autonomy, leading to limited independence and loss of resources to cope with everyday tasks. In this work, we analyse the status quo and potential influencing factors for the accomplishment of activities of daily living (ADLs) shortly after cancer diagnosis.

Methods: We recruited participants ages 4–18 years diagnosed with acute leukaemia or non-Hodgkin lymphoma. For the baseline analysis, we assessed (1) physical function limitations using the Activities Scale for Kids®, (2) exercise-related ADLs simulated with the Functional ADL Screen, (3) motor performance using the Motor Performance in Paediatric Oncology test and (4) physical activity (PA) level measured using an accelerometer.

Results: We conducted the baseline assessment 19.2 ± 12.6 days post-diagnosis in 41 patients. All participants reported functional limitations in ADLs and PA. Motor performance was reduced for all abilities. Cumulative steroid dose was negatively correlated with hand grip strength ($r = -0.50$, $p = 0.009$).

Conclusion: Shortly after diagnosis of paediatric cancer, patients experience various physical impairments that can be counteracted with regular, instructed exercise interventions.

Abbreviations: ADLs, activities of daily living; ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; ASK/ASKp, Activities Scale for Kids/Activities Scale for Kids, performance version; BMI, body mass index; MET, metabolic equivalents; MOON, Motor Performance in Paediatric Oncology; MVPA, moderate-to-vigorous physical activity; NA, not applicable; NHL, non-Hodgkin lymphoma; PA, physical activity; WHO, World Health Organization.

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KEYWORDS

activities of daily living, childhood cancer, leukaemia, motor performance, non-Hodgkin lymphoma, physical activity

1 | INTRODUCTION

According to international cancer registries, each year ~285,000 children ages 0–14 years are diagnosed with cancer worldwide (Steliarova-Foucher et al., 2017). Acute leukaemia and non-Hodgkin lymphoma (NHL) are the most prevalent malignancies in childhood and adolescence. Each year ~2200 children and adolescents are diagnosed with cancer in Germany. Of these, ~700 are registered with leukaemia (Erdmann et al., 2020) and ~160 with NHL (Burkhardt et al., 2018). Paediatric (<18 years) cure rates have increased through improved medical treatment regimens to 82% for a 15-year survival for all cancers, with 90% for leukaemia and 86% for NHL (Erdmann et al., 2020). However, drawbacks for survival are negative long-term effects of the disease and treatment, including cardiovascular diseases (Scholz-Kreisel et al., 2017), obesity (Oeffinger et al., 2003), osteoporosis (Marcucci et al., 2019), cancer-related fatigue (van Deuren et al., 2020), decreased quality of life (QoL) (Rueegg et al., 2013) and pain associated with cognitive, social and physical impairments (Tonning Olsson et al., 2021). Furthermore, burdensome short-term adverse effects immediately after diagnosis and initial treatment include anaemia, muscle pain, exhaustion and nausea (Bryant, 2003). In connection with recurring hospital stays, these factors can seriously impair an essential aspect for healthy development: the child's natural instinct for movement and play (Ginsburg et al., 2007).

Although these adverse effects appear early after diagnosis, their influence on patients' physical activity (PA) and activities of daily living (ADLs) has not been studied sufficiently. The loss of daily PA can result in reduced physical fitness and motor performance during and shortly after treatment (Braam et al., 2016; Götte et al., 2015; Hamari et al., 2020; San Juan et al., 2008; Thorsteinsson et al., 2017) and often persists throughout survivorship (Antwi et al., 2019; Howell et al., 2018; Ness et al., 2009; Yildiz Kabak et al., 2019).

During intense therapy, young patients experience impairments and burdens that can restrict their autonomy, mobility and self-determination (Marcus, 2012). Additional dependence on help with usually simple activities that satisfy basic human needs on a physical or psychological level (Juchli, 1993) can aggravate this situation. Parents of children and adolescents with cancer describe a spiral of physical inactivity, into which patients are drawn after diagnosis. Movement restrictions as a result of the hospital environment and commencing treatment were identified as factors for the decline of PA. As consequences of these restrictions, parents report low motivation, isolation and loss of independence (Grimshaw et al., 2020). During inpatient rehabilitation (Taguchi et al., 2018) and among childhood cancer survivors (Ness et al., 2005), the majority needs support when performing ADLs, and the demand for interventions is high.

Several studies have shown that, during and after acute treatment, reduced muscle strength occurs in children and adolescents (Deisenroth et al., 2016; Gocha Marchese et al., 2003; Götte et al., 2015; Schoenmakers et al., 2006). We hypothesise that muscular deficits as well as a sudden decrease in PA can potentially limit the autonomous ADL accomplishment early after treatment initiation. Increased muscle strength and regular PA are associated with coping with ADLs (Tanimoto et al., 2012) and thus can provide the greatest possible autonomy and mobility during treatment. However, little is known about the functional impairments affecting ADLs and PA close to diagnosis. These data are important for the conception and implementation of targeted exercise interventions to counteract early decline. Furthermore, factors that may influence these early side effects (e.g., corticosteroids and length of in-hospital stays) must be identified.

The aim of this work is to present the status quo for ADL accomplishment shortly after a diagnosis of acute leukaemia or NHL during childhood and adolescence to fill this previous gap of knowledge. We also analyse the status of motor performance, including coordination and muscle strength, PA level and the influence of steroids during the first weeks of intensive treatment.

2 | METHODS

2.1 | Study design and participant recruitment

In this article, we present cross-sectional data on the baseline assessment of the ActiveADL Study ('Effects of a Specific Strength Training on the ADLs for Paediatric Cancer Patients with Leukaemia and NHL', ClinicalTrials.gov: NCT03934060), a bicentric randomised controlled trial with paediatric cancer patients shortly after diagnosis at the Children's Hospital Schwabing and at the Dr. von Hauner Children's Hospital in Munich between September 2017 and June 2020. Eligible patients were aged 4–18 years with primary or secondary diagnosis (5 years post-primary tumour) of acute lymphoblastic (ALL) or myeloid leukaemia (AML) or NHL. Exclusion criteria were medical contraindications for PA post-diagnosis (e.g., thrombosis, high risk of bleedings or fractures), missing German- or English-language abilities and a change of hospital during the first weeks of treatment. The study protocol adheres to the ethical guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of the TUM School of Medicine, Technical University of Munich (TUM; 25/17 S) and of the University of Munich (18-323). The study content was communicated orally and in writing to eligible patients. Written informed consent to participate in this study was provided by the children's legal guardian.

Until the date of the baseline assessment, all participants were entitled to standard care physiotherapy but did not receive any exercise intervention. Physiotherapeutic measures shortly after diagnosis included mobilisation of the participants after catheter implantation or intensive medical treatment as well as respiratory therapy and fall prevention.

2.2 | Assessments and outcomes

The baseline assessment, which took place in the hospital (patient, day or waiting room) during the first intensive treatment period and immediately after study recruitment, included four outcome parameters: (1) the self-reported Activities Scale for Kids© (ASK), (2) the Functional ADL Screen with everyday tasks, (3) the Motor Performance in Paediatric Oncology (MOON) test and (4) PA quantified with an accelerometer (distributed at the first outpatient period for seven consecutive days). The participants' exercise capacity was verified by a physician before the assessment. Adverse events during and immediately after the assessment were noted with regards to the study of Gauß et al. (2021). The tests were also performed with an infusion stand. Based on our previous investigations, 60–90 minutes were estimated for performing the ASK, Functional ADL Screen and MOON-test.

2.3 | Self-reported ADLs

To investigate ADL accomplishment, we used the ASK performance version (ASKp) in German (Young, 2011). The 30 items, designed specifically for children ages 5–15 years, evaluate physical limitations caused by muscular disorders and describe the actual longitudinal changes in physical functions (Young et al., 2000). Seven sub-domains characterise (1) personal care, (2) dressing, (3) other skills (e.g., personal care for medical needs and printing/writing), (4) locomotion, (5) play, (6) standing and (7) transfers. Each item is scored on a 5-point ordinal scale with a rating range of 0–4, where 4 = *all of the time* and 0 = *none of the time*. If no reply is possible for an activity item, a 'not applicable' (NA) response could be selected. The participants answered the questions during their inpatient stay

retrospectively for 7 days. We calculated the ASKp score using the developer's method (Young, 2009). The prerequisite for the analysis was 23 valid items; NA responses were not considered. A total score of 100 indicates no physical limitation and, therefore, unrestricted ADL performance. Because of the cohort distribution, we also collected ASKp data from participants aged <5 and >15 years. Assistance with answering the questions provided by the parents or investigator was allowed and already has been validated, as well as the external assessment from the guardians (Young, 2009). The ASK has been used previously in paediatric oncology (Lawitschka et al., 2021; Piscione et al., 2014). Healthy cohorts also have been investigated (Costi et al., 2020; Plint et al., 2003), but age- and gender-specific reference values have not yet been published.

2.4 | Functional ADL Screen

As shown in Figure 1, we developed a test battery with seven everyday tasks to objectively verify the exercise-related ADLs in the ASK. The individual tasks, which simulated a chronological daily routine, were measured in the following order: (1) getting up from the floor, (2) putting on clothes, (3) putting on shoes, (4) carrying heavy objects, (5) climbing stairs, (6) pouring a drink, and (7) lying down on the floor. To assess the quality of movement execution, we used a scale of 0–4 for each task, with 0 = *movement not feasible*; 1 = *movement only feasible with help*; 2 = *independent movement only feasible with pauses and great difficulties*; 3 = *independent movement feasible with slight difficulties* and 4 = *uninterrupted course of the movement without limitations*. A total score of 28 indicates no functional limitations in ADL performance. This additional objective test complemented the subjective assessment of the participants by the ASK. The Functional ADL Screen has not been tested for quality criteria. Deficits in the practical ADL accomplishment could thus be identified at an early stage. Completing the Functional ADL Screen requires ~20 min.

2.5 | Motor performance

We complemented the ADL assessments with the MOON-test to evaluate motor performance (Götte et al., 2013). Eight test items

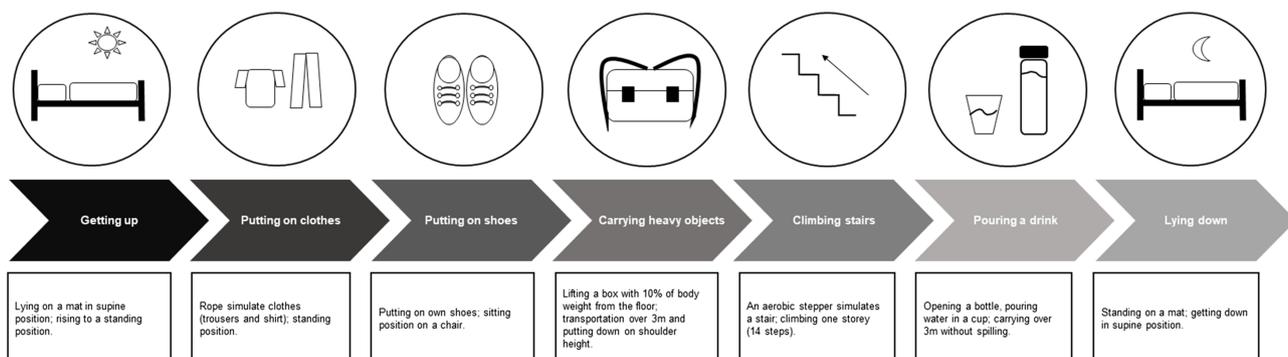


FIGURE 1 Scheme of Functional activities of daily living (ADL) Screen

examine motor abilities (e.g. coordination, speed, flexibility and strength): (1) inserting pins (hand-eye coordination under time pressure); (2) static stand (static balance/whole-body posture on a wooden bar); (3) reaction test (speed/reaction with optical stimuli); (4) throwing at a target (coordination with upper-extremity precision); (5) stand-and-reach (flexibility of hamstring and erector spinae muscles); (6) medicine ball shot (upper-extremity explosive muscle strength); (7) sit-to-stand (muscular endurance legs); and (8) hand-held dynamometry (isometric maximum hand grip strength). The test battery requires an average of 30 min to complete. We compared our data with age- and gender-specific reference values (Götte et al., 2013; McQuiddy et al., 2015; Metzinger, 2017). Except for static stand, a negative difference on a single test item represents a result below the reference value. For static stand and stand-and-reach, we calculated absolute differences to reference values, whereas we presented percentage of deviations for all other items.

2.6 | Physical activity

We assessed daily PA using the accelerometer Move 3 (movisens GmbH, Karlsruhe, Germany). We instructed the participants to wear the device on the right-hip side during daytime and to remove the device only for night-time sleep. Based on the published research on valid accelerometry in children, we included records with ≥ 4 days of ≥ 8 h/day of wear time (Burchartz et al., 2020). Move 3 assesses triaxial movement accelerations with a frequency of 64 Hz and a measurement range of ± 16 g (movisens GmbH, 2018). We used the algorithm of the DataAnalyzer software (version 1.13.16) to calculate the parameters for step count, amplitude of moderate-to-vigorous PA (MVPA), body position and wear time. This algorithm considers activity-based regression models to calculate motion-related energy expenditure depending on sex, age, weight, and height. The raw sensor data are based on 3D acceleration, temperature and atmospheric air pressure. Metabolic equivalents (METs) describe PA intensity, including the amount of consumed oxygen per kilogramme of body weight per minute. One MET has been defined as the consumption of 3.5 mL oxygen/kg/min sitting at rest (Jetté et al., 1990). MVPA is ≥ 3 METs. The inclination obtained from the acceleration was used to classify body position. The output interval was defined with 60 s. Wear time was calculated in 30 s intervals. Data on the validity of this device have been published previously. Compared to devices analysing raw data in form of counts in combination with single regression models, the Move 3 estimates activity-related energy expenditure more accurately (1.5–15 times lower relative differences to calorimetry reference values) in daily life activities of moderate intensity and reliably detects gait speeds (Anastasopoulou et al., 2014; Fiedler et al., 2021).

2.7 | Anthropometric and clinical data

We extracted anamnestic and anthropometric data, as well as disease-related information (e.g. age, cancer type, diagnosis date and

treatment regimen), from patient hospital records. For each participant, we calculated oral and/or intravenous cumulative steroid dose until the day of baseline assessment, including dexamethasone, prednisolone and methylprednisolone. Intrathecal steroid administration was not considered due to the low systemic effect. We measured anthropometric data (body weight and height) during a routine examination with patients wearing light clothes without shoes (scale seca 701, stadiometer seca 216; seca GmbH & Co., Hamburg, Germany). We calculated body mass index (BMI) as a ratio of body weight in kilogrammes and height in metre squared. The BMI z-score represents the standard deviation score of a German reference population and considers age- and gender-specific characteristics (Kromeyer-Hauschild et al., 2001). BMI categories were underweight (BMI z score ≤ -1.281 ; ≤ 10 th percentile) and overweight (BMI z score ≥ 1.281 ; ≥ 90 th percentile).

2.8 | Data analysis

We performed the statistical analysis using IBM SPSS (version 25) and designed the graphs using GraphPad Prism (version 9). Participants with < 4 days of at least 8 h/day of valid accelerometer data were excluded from the analysis. Descriptive analysis implied numbers and frequencies for the categorical and mean and standard deviation for the continuous variables. With the present sample size, median and range were also presented to assess the skewness of the distribution.

For the MOON-test items, we analysed the differences from the reference values using one sample *t* test with 90% confidence intervals considering the exploratory study design. For the items static stand and sit-to-stand, we used the Wilcoxon signed-rank test as the non-parametric alternative due to missing normal distribution. We used the Mann-Whitney *U* test to analyse the differences between the male and female participants and Pearson's correlation coefficient to examine the relationship between age and step counts. For all other correlation analysis, we used the non-parametric Spearman's *r*. Cohen's (1988) conventions were used to interpret the effect size of the correlation coefficient *r*. The criterion for statistical significance was $p \leq 0.1$. We performed the data analysis in consultation with the Institute of Medical Informatics, Statistics, and Epidemiology of TUM.

3 | RESULTS

3.1 | Participants

During the 34-month recruitment period, we screened 70 patients with a diagnosis of ALL, AML or NHL across both study sites. Among these, 29 children were not eligible according to the inclusion criteria. Overall, 41 patients were considered eligible for the study. The CONSORT diagram for recruitment is presented in Figure 2.

We achieved a recruitment rate of 100%, because all patients approached agreed to participate and were included after diagnosis

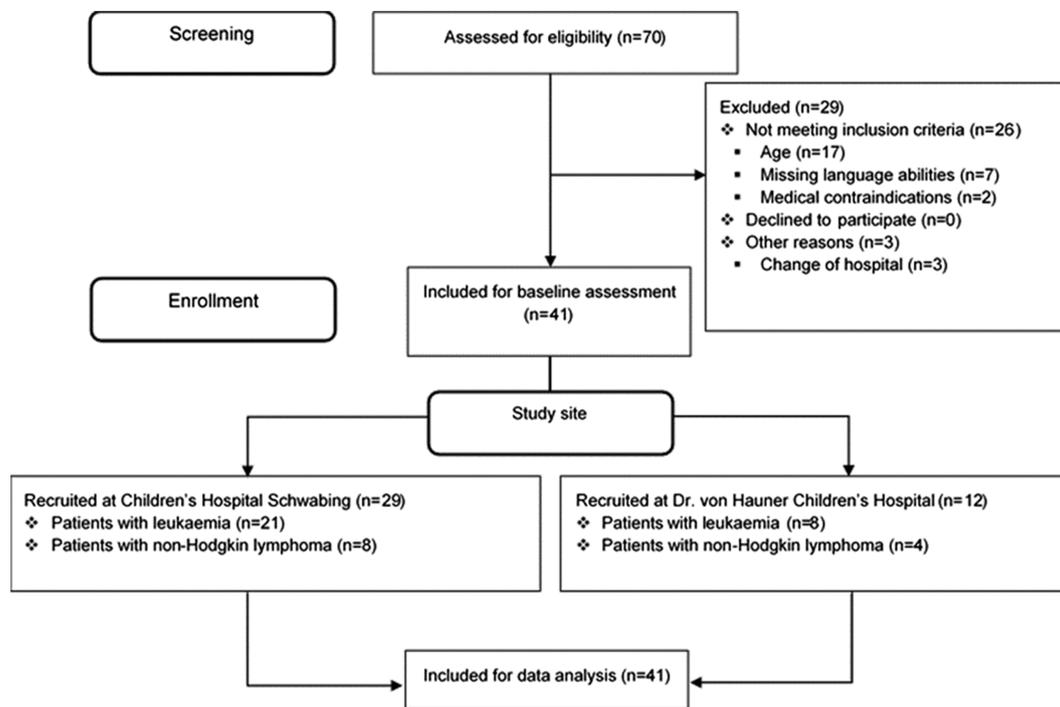


FIGURE 2 CONSORT diagram of recruitment. Medical contraindications were pneumonia/sepsis with long-term ventilation and intussusception with biliary colic

(15.1 ± 10.2 days; range 3–52 days). Patient characteristics (mean age 10.0 ± 4.0 years) are shown in Table 1.

Male participants represented 66% ($n = 27$) of the total cohort. Overall, 61% ($n = 25$) of the children were diagnosed with ALL, followed by 29% ($n = 12$) with NHL, and 10% ($n = 4$) with AML. We included two participants (5%) diagnosed with a second primary cancer eight and 15 years after primary diagnosis, respectively. The mean BMI z-score was -0.4 ± 1.2 ; 76% ($n = 31$) were of normal weight, 17% ($n = 7$) were underweight, and 7% ($n = 3$) were overweight. Until the baseline assessment, all participants had received their first doses of chemotherapy. A total of 38 participants (93%) had received steroids.

3.2 | Outcomes analysis

We conducted the baseline assessment 19.2 ± 12.6 days (range 6–56 days) post-diagnosis. No adverse events occurred during or immediately after testing. All participants answered the ASK, with 26 requiring adult assistance (help with reading or answering some or most questions) to complete the questionnaire (83% of children ages 4–10 years). For 30 participants, the ASK items were subjectively answered by self-report and 11 were objectively assessed by their parents (91% of children ages 4–10 years). The participants reported specific functional limitations: 46% ($n = 19$) were unable to perform daily body care; 24% were unable to climb stairs ($n = 10$); and 49% were unable to stand still for 10 min without resting ($n = 20$). The

Functional ADL Screen was measured in 40 and the MOON-test in 41 participants, respectively; valid PA data were available for 33 participants.

The results for ASK, the Functional ADL Screen and PA are shown in Table 2. The sub-group analysis (study site, tumour type, treatment protocol and age groups) did not reveal any significant differences. As shown in Figure 3, the male participants reached a higher total ASK score than did the female participants (mean 67.6 ± 17.7 vs. 55.2 ± 18.5 ; $p = 0.041$). In addition, the MVPA was higher among the male participants (mean 26 ± 20 min vs. 4 ± 5 min; $p < 0.001$). For the accelerometer (see Figure 4), age negatively correlated with mean step counts per day ($r = -0.61$; $p < 0.001$), representing a strong correlation (Cohen, 1988). Older participants tended to achieve a lower number of steps.

The results for motor performance are presented in Table 3. For the sub-domains hand-eye coordination ($p = 0.005$), speed ($p = 0.001$), flexibility ($p < 0.001$), muscular explosive strength ($p < 0.001$), legs' muscular endurance ($p < 0.001$) and hand grip strength ($p < 0.001$), the cohort scored significantly below the reference values; 88% ($n = 33$) scored below the reference values for hand grip strength, as did 96% ($n = 24$) for muscular explosive strength and 76% ($n = 31$) for flexibility. Figure 4 illustrates the significant negative correlations between cumulative steroid dose and hand grip strength (right hand, $r = -0.50$, $p = 0.009$; left hand, $r = -0.43$, $p = 0.03$), as well as the relationship between inpatient days until baseline assessment and flexibility ($r = -0.53$, $p < 0.001$), representing moderate to strong associations (Cohen, 1988). The ASKp score negatively

TABLE 1 Patients' characteristics

Characteristics	N (%)	M ± SD	Median	Range
Age at inclusion (years)	41 (100)	10.0 ± 4.0	9.3	4.3 to 17.5
Gender and age (years)				
Male	27 (66)	10.1 ± 3.9	10.1	4.4 to 17.5
Female	14 (34)	9.8 ± 4.4	8.0	4.3 to 17.1
Days post-diagnosis	41 (100)	15.1 ± 10.2	12.0	3 to 52
Inpatient days until baseline assessment	41 (100)	18.8 ± 11.1	15.0	7 to 48
BMI (kg/m ²)	41 (100)	17.0 ± 4.1	15.9	12.1 to 35.1
BMI z-score	41 (100)	-0.4 ± 1.2	-0.4	-3.5 to 3.1
Tumour type and age (years)				
ALL	25 (61)	8.9 ± 3.9	8.3	4.3 to 17.1
AML	4 (10)	13.3 ± 2.8	13.2	10.8 to 16.1
NHL	12 (29)	11.0 ± 3.9	12.2	6.1 to 17.5
Second primary cancer ^a	2 (5)			
Treatment				
Chemotherapy	41 (100)			
Cumulative steroid dose until baseline assessment (mg/m ²)	34 (83)	728 ± 625	474	7 to 2,835
Treatment protocol ^b				
AIEOP BFM ALL	17 (41)			
CoALL-08-09	8 (20)			
EsPhALL2017/COGALL1631	1 (2)			
AML-BFM	4 (10)			
NHL-BFM	11 (27)			
Medical brace ^c	1 (2)			

Note: Sex, age, steroid administration (oral and/or intravenous, not intrathecal), inpatient days and disease-related information were determined from hospital records. BMI z-score was calculated using sex- and age-adjusted reference values (Kromeyer-Hauschild et al., 2001).

Abbreviations: ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; NHL, non-Hodgkin lymphoma; M, mean; SD, standard deviation; N, number; BMI, body mass index; kg, kilogramme; m², square metre; mg, milligram.

^aParticipants who were diagnosed with a second primary cancer >5 years after first treatment: $n = 1$ ALL → NHL after 15 years; $n = 1$ NHL → different type of NHL after 8 years. The participants had completely recovered and had no limitations or long-term effects of the primary tumour.

^bTreatment protocols in detail: AIEOP BFM ALL (AIEOP BFM ALL 2009, AIEOP BFM ALL 2017), NHL-BFM (NHL-BFM Register 2012, B-NHL-BFM 2013), AML-BFM (AML-BFM Register 2017, AML-BFM 2012, AML-BFM 2019).

^cMedical brace was necessary in case of osteoporotic vertebral compression fractures in one patient. This limited the mobility in the upper body during the assessment.

correlated with cumulative steroid dose ($r = -0.50$, $p = 0.02$). Participants with higher cumulative steroid dose show reduced hand grip strength and achieve a lower ASKp score, respectively.

4 | DISCUSSION

The analysis of the ActiveADL cohorts reveals multifunctional impairments in self-reported ADLs, motor performance and PA shortly after a diagnosis of ALL, AML or NHL. To our knowledge, the data are the first analysed to this extent regarding the potential association of cumulative steroid dose and muscle strength in this population.

All participants reported ADL functional limitations at baseline assessment. Compared to the only paediatric oncology cohort in the published literature, albeit with bone tumours during maintenance

therapy ($n = 21$; mean age 14.6 years; 2.1 ± 1.6 years after tumour resection surgery), our participants' mean ASKp scores were lower (66.5 ± 19.3 vs. 79.6 ± 22.0) (Piscione et al., 2014). In addition, in comparison with a healthy student cohort (mean age 11.0 ± 2.9 years; ASKp score 89.1 ± 10.6), our participants' self-reported physical function was limited (Costi et al., 2020). There were neither adverse events nor any withdrawals during the Functional ADL Screen. Even under the participants' low individual physical capacity and in the clinical setting, this screen's 7 items simulated realistic everyday tasks. In addition, this screen specifically and practically reproduced individual ASK items, thus complementing the participants' self-reports and the parents' external assessments.

The subjectively reported limitations in the ASK were not as pronounced in the Functional ADL Screen. There was a potential ceiling effect because 30 participants (75%) scored the maximum of

TABLE 2 Results of ADL outcome parameters and physical activity

	N (%)	M ± SD	Median	Range
Self-reported ADL^a				
ASKp score (max. range 0–100)	25 (61)	66.5 ± 19.3	72.3	15.2–92.5
Self-reported				
Externally assessed	6 (15)	67.5 ± 26.1	75.0	15.2–86.2
Locomotion support indoor/outdoor ^b	6 (15)	59.8 ± 25.6	61.6	15.2–88.9
ASK total score (max. range 0–100)				
Self-reported	30 (73)	65.2 ± 16.5	67.1	22.5–92.5
Externally assessed	11 (27)	58.5 ± 24.0	71.9	15.2–92.5
Locomotion support indoor and/or outdoor ^b	13 (32)	56.2 ± 22.0	56.3	15.2–88.9
Functional ADL Screen				
Total score (max. range 0–28)	40 (98)	26.5 ± 3.9	28.0	11–28
Physical activity^c				
Mean MVPA per day (min)	26 (63)	17.0 ± 19.0	10.0	0–62
Week maximum MVPA (min)	26 (63)	31.0 ± 33.0	20.0	0–132
Mean step count per day	33 (80)	3,126 ± 1,834	2,668	219–6,300
Steps per day (week maximum)	40 (98)	4,694 ± 2,560	3,710	566–9,891
Wear time accelerometer (days)	33 (80)	6 ± 1	6	4–7
Off-ratio accelerometer (%)	33 (80)	52.4 ± 11.1	54.0	19.0–71.4
Body position^c				
Lying (h)	33 (80)	4:17 ± 2:46	3:58	0:33–10:57
Standing/sitting (h)	33 (80)	6:59 ± 2:17	6:41	1:21–10:31
Walking (h)	33 (80)	1:14 ± 3:03	0:38	0:03–18:09

Abbreviations: ADL, activities of daily living; ASK/ASKp, Activities Scale for Kids/Activities Scale for Kids performance version; h, hours; M, mean; min, minutes; MVPA, moderate-to-vigorous physical activity; SD, standard deviation; N, number.

^aAccording to the specification of the developer, the prerequisite to calculate the ASKp score was 23 valid answers (Young, 2009). Twenty-five participants met this criterion. ASK total score considered all responded items regardless of the number of valid answers. External assessment of ASK questionnaire through legal guardians was possible.

^bIndicated resources for locomotion were wheelchair, hand and knees, and carried by parents.

^cValid accelerometer data with records of ≥4 days with ≥8 h/day were analysed for 33 participants. This minimum requirement meant an off-ratio of 81%. The company-specific algorithm enabled MVPA calculation for 26 participants >6 years of age.

28 points. An insufficiently complex test battery or the distorted participants' self-assessments could be possible reasons. Further, the confounders related to self-reported data also could be an issue. In general, individual behaviour and attitude, social desirability, cognitive ability and other environmental factors can influence the validity of children's self-reports (Klesges et al., 2004). We therefore assume that differences in self-perception and in the ability of the participants to assess themselves could potentially influence the gender-specific differences in ASK results. For the total ASKp score, the descriptive analysis showed differences between the participants' self-reports and their parents' assessments. Parents may compare their children's current situation after diagnosis with their physical functionality before treatment. A similar observation has been seen in an analysis of QoL for survivors of paediatric haematopoietic stem cell transplantation, in which the parents rated QoL lower than did the children themselves (Parsons et al., 2012).

Moreover, the specifics and surrounding conditions of cancer treatment could influence the ASK results, especially the items with

NA answers, perhaps because the patients are isolated in their rooms, adhere to strict hygiene measures, do not meet peers and spend much time in the hospital. This reality rendered some of the requested ADLs, such as running around outside, meeting friends, sitting on the floor, walking/wheeling in crowded areas or doing usual jobs and chores impossible. Nevertheless, it is probable, that intensive chemotherapy and prolonged hospitalisation could negatively influence participation in ADLs and reduce patients' autonomy. Alizadeh Zarei et al. (2017) also found a similar outcome comparing young patients with various cancers (mean age 8.9 ± 1.9 years) with healthy children, showing that their participation in everyday life was limited, especially in diversity and enjoyment of activities and in satisfaction.

Deisenroth et al. (2016) has demonstrated significant deficits in all muscle groups among a paediatric cohort with various cancers (mean age 11.4 ± 4.1 years) in which they investigated isometric muscle strength 36.0 ± 20.5 days after diagnosis. Also Ness et al. (2015) has shown strength deficits at diagnosis of ALL that adversely impact health-related quality of life. In addition, Schoenmakers et al. (2006)

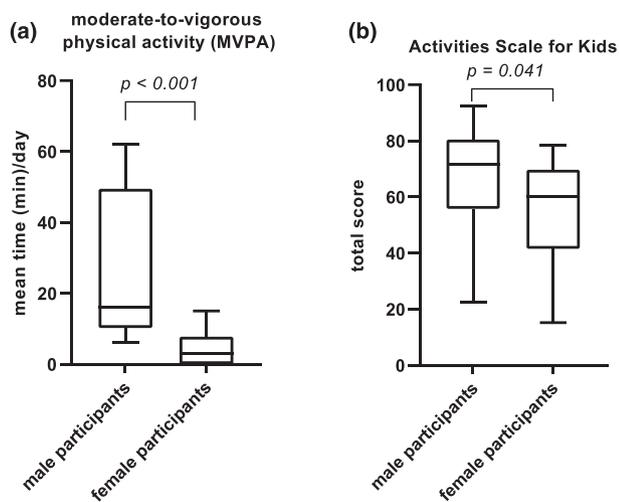


FIGURE 3 Differences between male and female participants regarding the outcome (a) mean moderate-to-vigorous physical activity per day, $n = 26$; and (b) Activities Scale for Kids© (ASK) total score, $n = 41$. Whiskers represent the minimum and maximum of the cases

has reported severe muscle weakness in children with ALL and NHL, particularly during the first 2 months of treatment. This weakness, which usually is reversible, was associated with steroids, vincristine, physical inactivity and neuropathy.

In the ActiveADL cohort, a correlation between cumulative steroid dose and hand grip strength and the ASKp score existed, respectively. Short-term side effects of glucocorticoid use in patients with ALL (e.g., myopathy, weakness and mood swings) depend on treatment duration and dosage (Inaba et al., 2010). Early exercise interventions and physiotherapy can prevent and treat muscle weakness for patients receiving glucocorticoids (Gupta & Gupta, 2013). However, we did not consider the efficacy of individual steroids in our analysis.

Many studies on accelerometry-assessed PA have shown large discrepancies in outcome parameters, cut points and wearing characteristics, rendering a comparison with other investigations difficult (Guinhouya et al., 2013). To exclude methodological limitations, we compared our data only with sensors that were attached to the participants' hips over a defined wear time. Paediatric cancer patients'

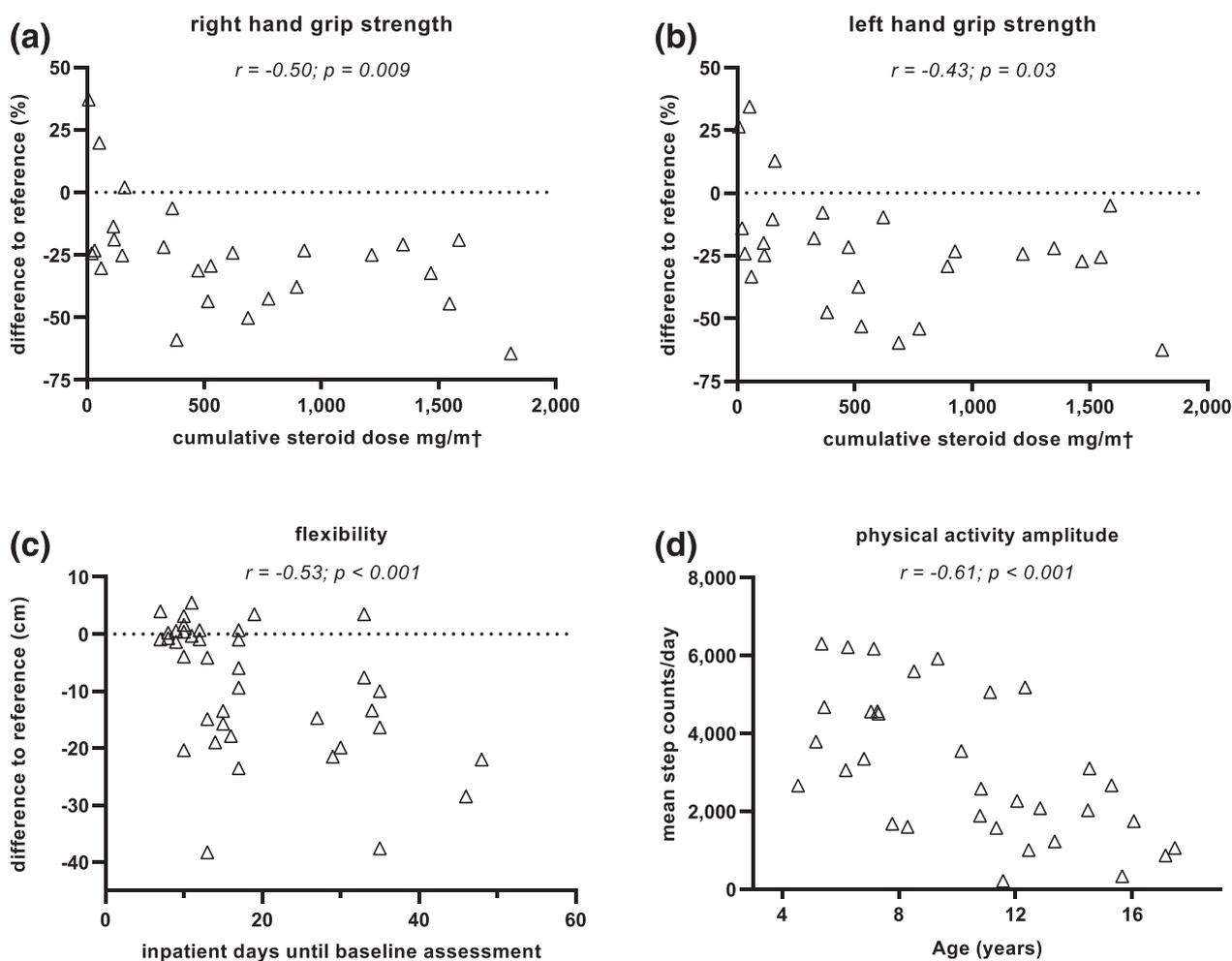


FIGURE 4 Scatter plots illustrate spearman correlation between cumulative steroid dose and (a) right hand grip strength, $n = 26$; (b) left hand grip strength, $n = 26$; and (c) between flexibility and inpatient days until baseline assessment, $n = 39$. A negative difference represents a result below the reference value. Pearson correlation (d) between mean step counts per day and age, $n = 33$

TABLE 3 Results of the MOON-test compared with age- and gender-specific reference values

Motor ability	Test item	N (%)	Differences to reference values (%)					n scoring below reference values (%)
			M ± SD	Median	Range	p	90%CI	
Eye-hand coordination	Inserting pins (time in s)	41 (100)	-14.5 ± 31.1	-9.2	-136.6 to 29.8	0.005	(-22.7, -6.4)	29 (71)
Static balance ^c	Static stand (ground contacts) ^d	34 (83)	9.2 ± 49.0 ^c	-0.2	-10.9 to 282.7	0.527 ^b	(-5.0, 23.4)	17 (50)
Speed	Reaction test (time in s)	39 (95)	-14.1 ± 24.3	-12.8	-124.0 to 23.5	0.001	(-20.7, -7.5)	29 (74)
Upper-extremity coordination	Throwing at a target (hits) ^a	16 (39)	-16.5 ± 56.0	-37.5	-100.0 to 142.9	0.257	(-41.1, 8.0)	10 (63)
Flexibility ^c	Stand-and-reach (difference in cm)	39 (95)	-9.2 ± 11.6 ^c	-6.0	-38.28 to 5.48	<0.001	(-12.4, -6.1)	28 (72)
Muscular explosive strength	Medicine ball shot (distance in m) ^a	25 (61)	-25.1 ± 16.7	-20.0	-61.5 to 0.0	<0.001	(-30.8, -19.4)	24 (96)
Muscular endurance legs	Sit-to-stand (time s)	40 (98)	-35.5 ± 70.0	-21.9	-420.4 to 32.8	<0.001 ^b	(-54.1, -16.8)	31 (76)
Hand grip strength	Hand-held dynamometry (strength in kg) ^a							
	Right	33 (80)	-24.7 ± 21.2	-24.3	-64.3 to 37.1	<0.001	(-31.0, -18.5)	30 (88)
	Left	33 (80)	-22.7 ± 23.0	-23.2	-62.4 to 34.4	<0.001	(-29.5, -16.0)	30 (88)

Note: Sit-to-stand results were compared with unpublished age- and gender-specific student reference values ($n = 289$) in Munich (Metzinger, 2017). All other results were compared with the reference values of each single test items (Götte et al., 2013; McQuiddy et al., 2015). Static balance could only be measured in 34 participants, speed in 39, upper-extremity coordination in 16, flexibility in 39, muscular explosive strength in 25, muscular endurance legs in 40 and hand grip strength in 33, due to missing reference values or restricted health status.

Abbreviations: CI, confidence interval; cm, centimetre; kg, kilogramme; m, metre; M, mean; N, number; p, p value; s, seconds; SD, standard deviation.

^aBecause of published reference values, throwing at a target is limited to participants between 6 and 11 years of age, the test items medicine ball shot and hand-held dynamometry are limited between 6 and 18 years of age.

^bWilcoxon signed-rank test was used to calculate p value for median difference.

^cAbsolute differences to reference values were calculated, because values around zero lead to exaggerated percentage values.

^dA positive difference in static stand represents a result below the reference values, because it means a higher number of ground contacts of the free leg.

PA levels often decrease significantly during acute treatment due to disease- and therapy-related side effects (Braam et al., 2016; Winter et al., 2009). Rehorst-Kleinlugtenbelt et al. (2019) have conducted a comparable study with a Dutch cohort (median age 8.2 ± 4.7 years) with various types of cancer during acute therapy. The average MVPA per day (median, 10 ± 19 min vs. 4 ± 9 min) was higher, but the steps per day were lower ($2,688 \pm 1,834$ vs. $3,564 \pm 2,698$) for the ActiveADL cohort. Accordingly, the intensity of PA was potentially lower in the Dutch cohort (<3 METs). In general, the participants' PA was reduced at the initiation of intensive treatment. Only two participants (8%) in our study achieved the World Health Organisation's (WHO's) PA recommendation for an average of 60 min of daily MVPA for children and adolescents (Bull et al., 2020). Among the valid accelerometer measurements, there were three participants (12%) with only low intensity of PA (<3 METs) registered. These results support those of Kowaluk et al. (2019) for restricted PA among patients with hematologic malignancies (mean age 13.0 ± 1.5 years) undergoing treatment.

Another study among a German population using the ActiGraph accelerometer has shown low adherence to the WHO recommendations, even for healthy children and adolescents; of the 2694 participants, only 4% reached the WHO standard (Burchartz et al., 2021). The PA data illustrated that the exercise behaviour of the participants varies greatly between individuals. Depending on the state of health, outpatient therapy phases are used for regeneration. The majority of the participants also tried to integrate PA into their daily therapy routine at home. In our cohort, the parents and siblings were a decisive motivating factor.

According to our experience, physical or behavioural barriers to an active lifestyle during treatment, such as fear of injury, fatigue, motivational problems or an inactive environment (Ross et al., 2018), can potentially be reduced through education, motivational and varied exercise content, and parental support, as well as through multidisciplinary team support. Exercise interventions should achieve a certain level of PA and effort and consider children's individual motor capacities.

5 | LIMITATIONS AND STRENGTHS

The primary research proposal of the ActiveADL Study was to assess the intervention effect of an exercise programme. The analysis of the baseline data specifically presents the status quo of the participants at the beginning of treatment. However, the cross-sectional findings collected on functional limitations shortly after diagnosis close the existing research gap. Selection of the ActiveADL cohort was deliberate, because acute leukaemia and NHL are among the most common paediatric cancer types (Erdmann et al., 2020) and form a potential homogeneous group due to their systemic treatment without tumour surgery. Conclusions about the status quo for other cancer types cannot be made. The small number of participants as well as the skewed age and gender distribution limits a subgroup analysis of cancer types and a generalisation of the results. Thirty-four participants were recruited within the first 3 weeks after diagnosis. Intensive care treatments during the first inpatient stay, catheter surgeries, extensive diagnostics and unpredictable incidents led to the range of the recruitment period. The outliers achieved results within the standard deviation. For 30 participants, we collected single outcome parameters over several days because of their restricted physical capacity or the time constraints of their daily clinical routine. The estimated total time of 60–90 min to complete the tests was met by the entire collective. The parents' external ASK assessment limits the validity of the self-reported questionnaire. Valid PA measurements are related to the accelerometer's position around the centre of the body (Thiel et al., 2016). Therefore, we placed Move 3 on the hip. We noticed that the younger participants ($n = 5$, ages 4–7 years) felt more disturbed by the sensor on the hip. As a result, all of them refused the measurement. Limitations in wear compliance among children have been reported previously, resulting in the recommendation to use wrist sensors for this age group instead (Fairclough et al., 2016). Because of the accelerometer's given algorithm, the MVPA could be calculated only for those participants >7 years. The validation of the self-developed Functional ADL Screen was not a study objective, but served as an additional diagnostic measure of functional deficits at an early stage of therapy for the subsequent intervention. The findings on ADL accomplishment are based on the ASK data. For further application of the Functional ADL Screen in future studies, validation of this tool should be approached to obtain reliable results. In addition, the assessment of the Functional ADL Screen by two investigators could lead to bias.

The strength of our ActiveADL Study is the certainty that extensive measurements with various outcomes can be implemented immediately after diagnosis. As far as we know, this is the first study to assess ADL accomplishment shortly after diagnosis of ALL, AML or NHL. Moreover, data collection was carried out at two study sites over the entire period exclusively by two sports scientists. It is worth noticing, that the COVID-19 pandemic did not affect the data collection. Finally, the recruitment rate of 100% illustrates the willingness of patients and their families to participate in a structured exercise programme during early-stage treatment.

6 | CONCLUSION

Children and adolescents undergoing cancer treatment report a limited ability to perform ADLs in the clinical setting and during outpatient periods shortly after diagnosis. Disease- and treatment-related side effects in the first weeks of intensive treatment not only affect ADL accomplishment but can also lead to reduced motor performance and limited PA levels. Potential influencing factors are medication, particularly steroids, duration of inpatient stay and associated hospitalisation times as well as inactivity phases. We highlighted with our analysis, that exercise interventions are indicated and may potentially be beneficial for patients with acute leukaemia and NHL. As severe strength deficits tend to occur in paediatric patients shortly after diagnosis, a specific strength training may address this aspect and have positive effects. Longitudinal data analysis of the ActiveADL Study intervention should provide new insights. It is conceivable that the patients' autonomy concerning the ADL accomplishment during treatment could be preserved through targeted exercise as well as maintaining PA. Our results suggest that structured and holistic exercise therapy should be part of the standard care in departments of paediatric oncology in the long term (Gesellschaft für Pädiatrische Onkologie und Hämatologie (GPOH)/AG Netzwerk ActiveOncoKids (NAOK), 2021). Further intervention studies are needed to explore the effects of sports programmes independent of cancer type and functional impairments.

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CONFLICT OF INTEREST

All authors declare that the research was conducted in the absence of any commercial or financial relationship that could be construed as a potential conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available because of privacy or ethical restrictions.

AUTHORS' CONTRIBUTION

SK and MG conceived the study idea and designed and planned the study. DG and SK collected and managed the data. DG and SK conducted the analysis and prepared the first draft. IvL and IS provided medical supervision. IvL, RO-F and TF proofread the study concept. CP was involved in an advisory capacity with the study administration. All authors read and approved the final version of the manuscript.

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