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Exploring the Barriers and Facilitators to Physical Activity Behaviour in Older Adults With Intellectual Disabilities: Lessons From and for a Co-Design Study

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ABSTRACT

Background: Physical activity (PA) is one of the core components of healthy ageing. For older adults with intellectual disabilities (ID), PA is even more important because they often have a more sedentary and inactive lifestyle and more health problems than do older adults without ID. To promote PA, we explored personal and contextual barriers and facilitators to PA for this group.

Methods: We used a research-through-design approach with six older adults with ID in a specific care home facility. By applying co-design methods, older adults with ID, caregivers and other stakeholders were involved from the beginning in (1) listing barriers and facilitators, (2) exploring PA-promoting interventions and (3) adapting co-design methods to the target group.

Results: Our work resulted in a list of barriers and facilitators for the participants to perform PA, related to the personal characteristics of the participants, the provided PAs and the physical and social context. Further, a PA-stimulating intervention prototype and lessons learned regarding co-design with older adults with ID were developed. It became clear that a modular, adaptive intervention is necessary to accommodate the individual needs and wishes of older adults with ID. The same adaptive approach was required to meaningfully involve them in the research and design process.

Conclusions: Older adults with ID cannot be regarded as a homogeneous group, and there is no one-size-fits-all solution for promoting their PA. Basic components for an intervention can be provided, yet they always require adaptations to personal and contextual circumstances. The identified barriers and facilitators, intervention prototype and co-design lessons can provide guidance for creating tailored interventions.

1 | Introduction

People with intellectual disabilities (ID) often have a sedentary and inactive lifestyle, with only 9% (0%–46%) being sufficiently active according to the physical activity (PA) guidelines (Dairo et al. 2016). For older adults with ID (≥ 50 years) in particular, it was found that only 17% took 10 000 steps/day (Hilgenkamp, Reis, et al. 2012). Besides these low PA levels, their physical fitness has been found to be comparable to or even worse than that of adults without ID who are 20–30 years older (Hilgenkamp, van Wijck, and Evenhuis 2012). These poor physical fitness levels put them at a higher risk for decline in mobility and ability to perform activities of daily living and at a higher risk for early mortality (Oppewal and Hilgenkamp 2019). Older adults with ID also have a lot of health problems at a relatively younger age than the population without ID, such as high frailty levels (Schoufour et al. 2013), cardiovascular risk problems (Rimmer and Yamaki 2006) and chronic health conditions

(Draheim 2006). With the increasing life expectancy of adults with ID (Dolan et al. 2019), adding healthy years to their life is therefore an important aim.

As decades of research have indisputably proven the health benefits of PA, increasing PA of adults with ID is an important strategy for healthy ageing. However, it is not an easy task to support them in achieving and maintaining an active lifestyle. Following the socio-ecological model, it is essential to take into account factors at the intrapersonal, interpersonal and organisational levels to successfully intervene (Sallis et al. 2006). Examples of often observed personal barriers for PA are limitations in cognitive and physical functioning, health issues, lack of self-confidence, lack of skills, age-related problems and fear (Bossink et al. 2017; van Schijndel-Speet et al. 2014). Additionally, often mentioned contextual barriers are inaccessibility of locations, lack of inclusion and appropriate PA options, and limited human and financial resources (Salomon et al. 2019; van Schijndel-Speet et al. 2014). Although facilitators for performing PA are identified as well, such as social engagement with peers and friends, reward for participation, a fun component within activities, a good fit within everyday routines and having choices (Bossink et al. 2017; Salomon et al. 2019), altogether, the personal and contextual barriers significantly impact PA opportunities for older adults with ID.

To overcome these generic barriers and leverage the facilitators, it is essential to ensure that PA interventions are tailored to the context of use and the targeted users. Even though PA interventions specifically designed for people with ID were found effective in increasing PA and improving health (van Schijndel-Speet et al. 2017; McDermott et al. 2023), implementation in daily practice often remains difficult. There are limited financial resources, time of staff, motivation and abilities to execute the intervention and fit it into daily routines. Additionally, most of these interventions are not focused on older adults, who need age-appropriate interventions tailored to their specific challenges and opportunities.

To arrive at contextually and personally tailored interventions for older adults with ID, it is important to engage stakeholders in every phase of the development process using a co-design method (Melles et al. 2021; Sanders and Stappers 2012). This starts with discussing needs, wishes, barriers and facilitators. Furthermore, stakeholders can participate in defining intervention goals and requirements, brainstorming solutions, and testing and improving prototypes. Involving stakeholders helps designers gain a more intimate understanding of the end-users and the intervention's context of use (Kouprie and Sleeswijk Visser 2009), which helps them make fitting design decisions.

The aim of this study is to explore the barriers and facilitators of older adults with ID regarding PA in their home environment, including the challenges of implementing an intervention. In this co-design process, we collaborate with older adults with ID and their caregivers on designing an intervention that stimulates the older adults' PA. The second aim is to gain insight into how a co-design process can be fitted to older adults with ID. PA interventions have been co-created with older adults without ID (Leask et al. 2017). However, as far as we know, such a participatory process has not been done often before, and we expect that it will benefit the development, implementation and impact of future PA interventions for older adults with ID.

2 | Methods

2.1 | Study Design

Applying co-design methods to discover barriers and facilitators is a form of research-through-design (Stappers and Giaccardi 2017). Research-through-design is a non-linear, iterative approach that employs methods from the field of design to generate knowledge (Dalsgaard 2016). In this study, this included participatory design activities in which we explored the context, brainstormed solutions and produced prototypes in collaboration with older adults with ID, their caregivers and other experts. As research-through-design is a qualitative research approach, we use the COREQ checklist to give a more explicit and comprehensive report of our study (see Appendix SI for the full checklist; Tong et al. 2007).

2.2 | Participants

Participants were recruited through purposive sampling in a living arrangement for older adults with ID of healthcare organisation's Heeren Loo, located in Noordwijk in the Netherlands in 2022. After an introduction of the study by the caregivers, eight residents who met the inclusion criteria of being ≥ 50 years old and having a mild to moderate ID were approached to participate in one-on-one conversations. There were no exclusion criteria. An easy-to-read and visually supported information letter and consent form were used to help explain the study and the role of the participants. Six residents agreed to participate. Two residents declined because of the content of the activities and/or the expected time investment. Informed assent was provided by the residents and consent by their legal representatives. The study was approved by the Human Research Ethics Committee of Delft University of Technology (Approval Number 2126), and an agreement was provided by the healthcare organisation.

Of the six older adults (mean age 75 years; range 57–87) who participated, five lived in the same household, whereas one lived on another floor in the same building. The six participants displayed a wide range of interests and differed widely in their physical and cognitive abilities (Table 1) and how they wanted to be approached (e.g., direct, calm and playful). One participant displayed a high level of intrinsic motivation for PA, whereas three others had PA-related hobbies but otherwise responded negatively to PA in general. Communication skills varied, with one participant limited to simple one-word responses, whereas some others were able to express preferences and talk about earlier experiences. Physical abilities of the participants varied, with one participant being in a wheelchair, whereas three continuously or occasionally relied on a walker, and two were able to walk substantial distances without support (Gross Motor Function Classification System [GMFCS] 1–4). To complement the perspectives of the six participants and enrich our findings,

TABLE 1 | Participant characteristics.

Participants	Sex	Age	Walking aid	Hobby/activities
P1	M	73	None	Drumming, singing, dancing, visiting thrift shops and going to a daytime activity centre 4 days a week.
P2	M	80	Walker	Watching sports and knitting at the daytime activity centre.
P3	M	72	Walker	Making puzzles, crafting and going to a daytime activity centre 5 days a week.
P4	F	87	Wheelchair	Exercise class 2 times a week, reciting or singing old poems and songs.
P5	F	57	Occasionally	Drawing, singing, dancing, acting, performing PA with others and going to a daytime activity centre 3 days a week.
P6	M	80	None	Playing simple, sportive games (e.g., with balls) and going to a daytime activity centre 3 days a week.

we consulted caregivers and other experts involved in the care of the participants.

2.3 | Study Context

The living arrangement in this study is situated in a regular residential area. The residents live in a homely atmosphere with their own bedroom and preferably a private bathroom. The participants in this study received full-time care and/or guidance, and most of them participated in organised daytime activities on workdays. All research activities in this study were performed at the home or daytime activity centre of the participants.

2.4 | Data Collection

The data collection consisted of three phases. Most research activities (Appendix SII) were executed by a design researcher (first author), followed by analysis and reflection on the outcomes together with the other members of the team consisting of a design researcher (NV), human movement scientists (AO, JK) and a physiotherapist (MB). Parallel to these three phases, we actively adapted our methods to the wishes and abilities of the participants and reflected upon our co-design activities regularly. The physiotherapist of the participants, the innovation department and the speech therapist's Heeren Loo were consulted to gain more insight into existing interventions and into testing interventions with the participants. Over 9 months, the design researcher visited the participants' context 15 times, averaging 2 h per visit.

In the first phase of the study, the main goal was to improve our understanding of the residents' context and current (lack of) PA. Through observations, we learned about the current level of PA, PA initiatives that were already taken and adequate communication with the residents. We performed interviews with a physiotherapist, a speech therapist, caregivers at the daytime activity centre and the caregivers working in the living arrangement. In a brainstorming session, four caregivers, two designers and one PA expert explored barriers and facilitators to PA in the home and living environment and the perspective of the caregiver. The barriers and facilitators collected in this phase were verified and extended in the next phases of the study.

In the second phase, we performed multiple generative sessions (creative sessions) to improve our understanding of the needs and wishes related to PA. The sessions focused on (1) general interests and engagement through conversation starters (Figure 1) and testing interactions with music, storytelling, instructions and peers; (2) triggers for PA by exploring different types of products, games, sounds and things from their past; and (3) the role of other people in stimulating PA.

In the third phase, we used co-design activities to extend and verify the barriers and facilitators to PA from earlier phases and explored intervention opportunities. The participants tested multiple concepts, and based on this, a first prototype was developed. These directions were evaluated with emoticons and a conversation map. The map contained statements such as 'I liked the activity' or 'I got tired of the activity'. This resulted in design requirements for a PA intervention and the development of an improved prototype.

2.5 | Analysis

The Data, Information, Knowledge, Wisdom (DIKW) model from Ackoff (1989) served as a structured framework to thematically analyse our audio transcripts, session output, and notes and observations to identify barriers and facilitators of older adults with ID regarding PA in their home environment. The data collection was performed by the first author. The other researchers contributed to the transformation of raw data into information and knowledge through collaborative statement card analysis (Sanders and Stappers 2012).

First, we organised the data. Second, the raw data were filtered for relevance regarding barriers and facilitators to PA. The resulting relevant parts consisted of a collection of quotes from participants and insights or observations from the researchers' perspective ('Information'). Third, the quotes and observations were interpreted, combined and translated into barriers or facilitators to PA ('Knowledge') (Table 2 and Appendix SIII). Finally, the barriers and facilitators were connected, and insights from the co-design activities were added. We applied this knowledge in a prototype intervention to stimulate PA for older adults with ID ('Wisdom').

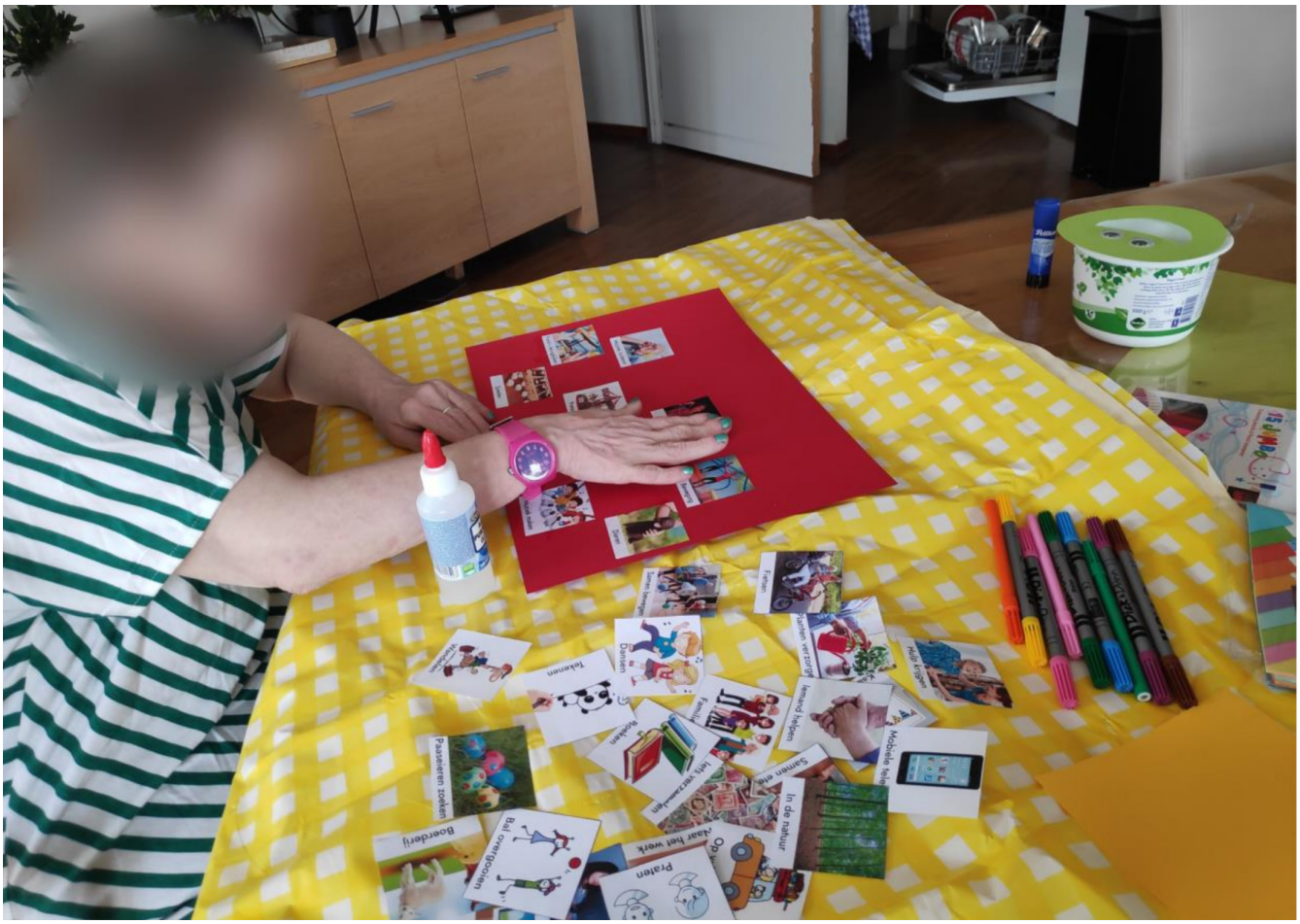

FIGURE 1 | Participant making a collage of activities she enjoyed doing, related to research activities in Phase 2.

TABLE 2 | Example of how filtered data and information were combined into a barrier (knowledge), which was translated into an intervention criterion (wisdom).

Quotes, notes or observations	Barrier	Intervention criterion
'With bowling. If you can do it well, I've done it a few times, you must aim well. I do not do that anymore, I'll fall over.'—quote P2 (data) 'I did enjoy walking once, but now I do not do it anymore, because it hurts my leg. I had fallen on my hip. So now I walk with a rollator.'—quote P3 (data) She talks a lot about how she used to do it, but not anymore, and about something that did not go well or has been lost—study note P4 (information) 'There is also one client who wants to move, but is not allowed to walk a lot, because her back is fixed. So finally, someone wants to move and now she is not allowed to ….'—quote employee daytime activity centre (data)	*Being less and less able and allowed to do PA due to age-related complaints. (knowledge)*	*The intervention needs to take age-related complaints into account, facilitating participation of people with different (physical and cognitive) abilities. (wisdom)*

2.6 | Trustworthiness

We applied several strategies to enhance the trustworthiness of our research set-up as suggested by Polit and Beck (2012), including evocative reporting and disclosing our quality-enhancing strategies in this paper. We used multiple data collection methods, and various expert stakeholders were consulted throughout the study. Transcripts of conversations were complemented with creative outputs, and resident perspectives were complemented with the perspectives and knowledge of the local caregivers, daytime activity centre caregivers and physiotherapist.

As people with ID sometimes have difficulty with forming and verbalising opinions (Shaw and Budd 1982), we put considerable effort in using suitable interviewing techniques, supporting material and consulting literature and caregivers. In addition, we repetitively performed a creative activity with the residents, reflected on the findings and then planned a new activity. Through this iterative process of member checking, persistent observation, reflexive note-taking and regular discussions with the research team throughout the whole process, the research team maintained a critical attitude, and the residents' voices were adequately represented.

3 | Results

The insights we gained during the three phases of data collection are translated into barriers and facilitators for the participants to perform PA, a PA-stimulating intervention prototype and lessons learned regarding co-design with older adults with ID. In the following paragraphs, we expand on our findings and cluster the identified barriers and facilitators to becoming physically active into three categories: (1) the personal characteristics of the participant and their ID, (2) their physical and social context or (3) the PAs that are provided (Figures 2 and 3).

3.1 | Main Barriers to Become Physically Active

Starting with the personal characteristics, we found that age-related health complaints, such as mobility issues, physical pains or low energy levels, are an important barrier for PA. These barriers resulted in being less able to (independently) perform PAs. 'I did enjoy walking once, but now I don't do it anymore, because it hurts my leg' (P3). For some clients, negative previous experiences prompted them to be more cautious and limit their activities. The physiotherapist emphasised that clients are often afraid to fall or experience pain, and participants confirm this. Interviews with the physiotherapist and observations at the home and daytime activity centres showed that participants are mostly inactive during the day. Most of them are not used to doing any PA and often prefer inactive behaviour. These personal barriers result in negative associations with PA and therefore a negative response to PA when suggested.

Looking at the residents' context, clients depend on others or need an external stimulus to get physically active, whereas caregivers experience a threshold to promote PA due to the participants' negative responses. Additionally, caregivers lack time, priority and sometimes personal motivation to integrate PA in the daily schedule. Not having the right materials or space to organise activities is also mentioned as an important barrier. Most residents cannot go outside without supervision because the care home is located on the edge of a residential area, with heavy traffic and many curbs.

These personal and contextual barriers cannot be seen separately from the PA itself. Although participants' lack of enjoyment of an activity may be partly attributed to their lack of motivation, the suitability of the activity itself plays an important role as well. Within this study, several activities were tested, and reasons for quitting or disliking the activity were often that the activity was not adapted to the participants' physical abilities, was cognitively too challenging or was not aligned with

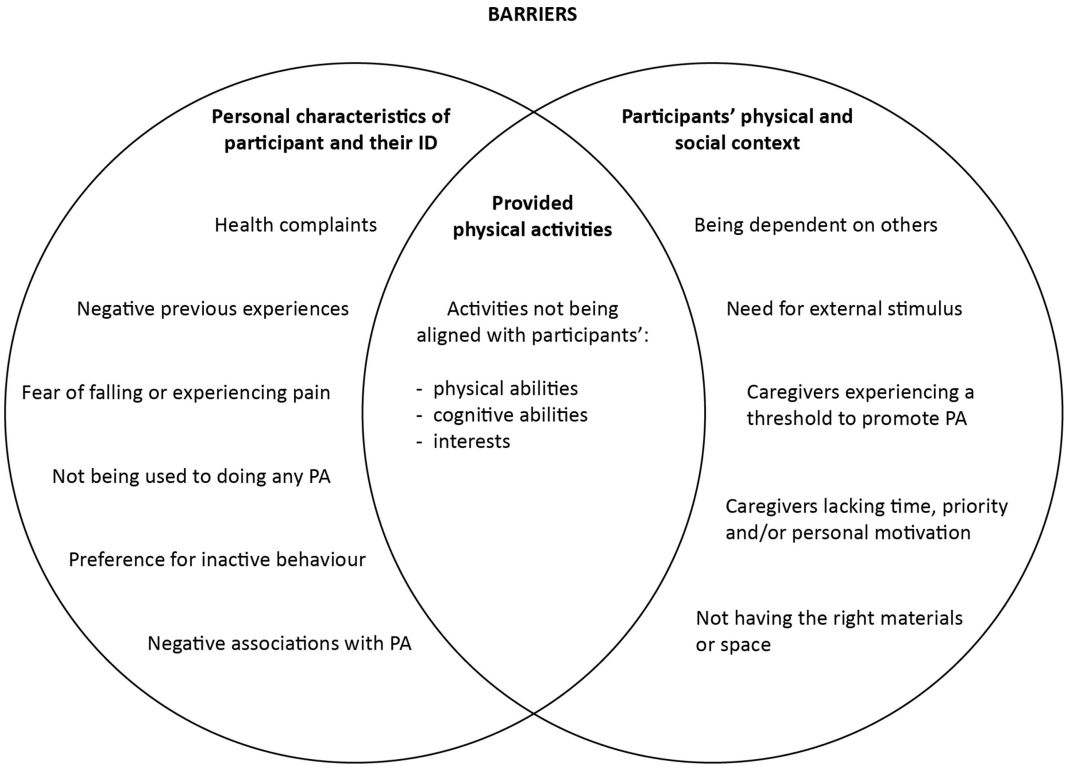

FIGURE 2 | Overview of barriers to become physically active in relation to personal characteristics, the context or both. ID: intellectual disability; PA: physical activity.

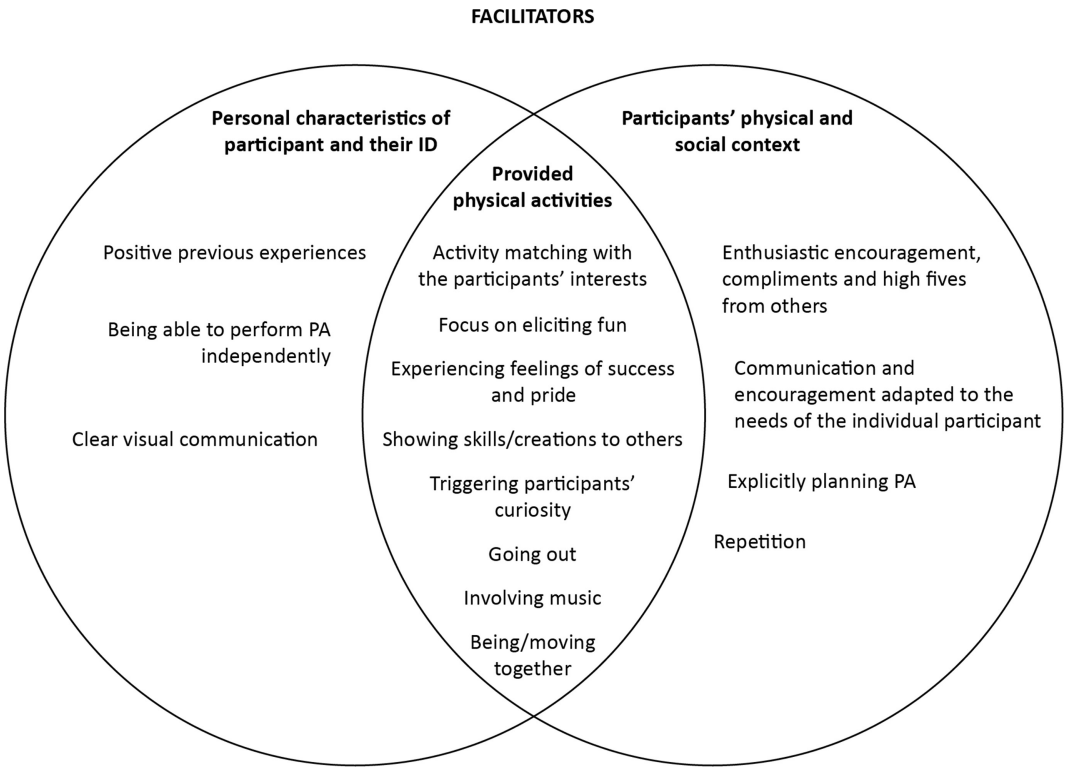

FIGURE 3 | Overview of factors that help to become physically active in relation to personal characteristics, the context or both. ID: intellectual disability; PA: physical activity.

the participants' interests. 'I don't like puzzles. Puzzles are a bit difficult for me' (P1).

3.2 | Main Facilitators to Become Physically Active

Where negative previous experiences appeared to be an important personal barrier, positive previous experiences served as a personal facilitator or motivator to perform PA. 'I once biked on a duo bike. That was really fun, the pedalling went very fast' (P5). Moreover, opposed to being dependent on others, being able to perform PA independently lowered the threshold to be physically active and to gather positive experiences. To achieve a positive (independent) experience, the activity should also be matched to the participants' abilities and thus, for example, should make use of clear visual communication. 'When it is my turn, I can tell by the light' (P2).

However, most participants were not able to perform tasks independently. While the participants were performing the PAs, the design researcher was always present and—to a greater or lesser extent—involved in the activities. Consistent with the dependence on an external stimulus, the researcher often stimulated the participants with practical and motivational assistance. Observations and interviews showed that enthusiastic encouragement, compliments and high fives from someone else were an effective method to persuade participants to start and continue PA. However, the correct approach differed per participant, so communication and encouragement adapted to the needs of the individual remain important. In addition, we observed that participants often ask which caregiver will be present and what is on the menu, and they also often refer to their own planning. Hence, explicitly planning PA could work as an effective facilitator for the residents as well, ideally with repetition to stimulate them to initiate activities themselves. 'I do notice that clients initiate or ask it more often once you have played games more often' (C2).

Participants were more eager to participate when the activity matched with their interests. For most participants, this meant that the focus should not be on PA but on eliciting fun, as the term 'physical activity' evoked negative associations and responses. An important aspect of this was to experience feelings of success and pride during the activity. 'Have you ever danced? Yes, yes! I have a lot of diplomas from my dance lessons' (P1). For some participants, it was extra fun if they could show their skills or creations to others. To motivate the participants to start PA, it helped to trigger their curiosity. Although the participants varied in their preferences, some triggers were common. For instance, going out was found to be motivating for some participants, involving music made all participants participate more actively and most participants preferred being or moving together. In practice, moving in duos seemed the best balance as more than two people made it overwhelming for most participants.

3.3 | Prototype Description

From the collaboration and interaction with the residents and their caregivers during the three phases of this study, we developed a prototype for a PA intervention (Figure 4). As is common in a research-through-design approach, the prototype functioned both as a tool to expand and validate our earlier findings and as a conceptualisation of our results.

FIGURE 4 | A concept visualisation of the MakiMove with three activities: (1) drawing, (2) throwing balls and (3) dancing to music.

Therefore, the prototype should not be interpreted as the only solution but should serve as an example of how our insights were translated into an intervention to improve PA in older adults with ID.

The prototype—named the MakiMove—is a large, vertical, modular game board with the aim of providing a positive experience for older adults with ID and simultaneously increasing PA by doing activities that require movement. The MakiMove prototype is modular, offering three activities (drawing, throwing balls and moving to music) with a variety of difficulty levels and the option to play alone or together. In addition, the MakiMove is designed as an affordable game board, which can easily be transported in and out of the room. More details regarding the MakiMove prototype are provided in Appendix SIV.

3.4 | Adjustments in Co-Design Methods

Our initial co-design methods were based on the work of Sanders and Stappers (2012). During the process, we adjusted our method based on intellectual functioning and behaviour of people with ID and our experiences with the participants. Below, we summarise these adjustments into four lessons learned from co-designing with older adults with ID.

First, when collaborating with this group, we recommend planning a prolonged period—and additional effort—to get to know the participants in an informal setting. More than customary in participatory approaches, a positive collaboration with this target group relies on confidence, acceptance and flexibility from both sides. In our research, we took extra care to address individual abilities, expectations and mood of the participants and adjusted our approach accordingly.

Second, people with ID have difficulty with abstract reasoning, like problem solving or thinking conceptually without concrete examples (Shogren and Turnbull 2010). Therefore, we introduced generative tools and detailed functional prototypes early in the process. Through these prototypes, our participants could try out things instead of talking about experiences, and we could observe their interactions with the prototypes and ask explicit questions about their experiences.

Third, people with ID have a slower pace of information processing and a shorter attention span (Shogren and Turnbull 2010), and we observed that the participants struggled with remembering and differentiating between options. When residents were presented with multiple options for an activity, we noticed some always selected the last option. In response, we limited the number of activities per session and evaluated them directly after or during the activity. After an activity, participants sometimes lost interest quickly or were exhausted and required a break.

Fourth, people with ID often have difficulty with being aware of their own thoughts and feelings and verbalising experiences (Shogren and Turnbull 2010). As this is a vital source of information in participatory research, we used a conversation map where participants could indicate their thoughts and feelings using a happy emoticon or sad emoticon (Figure 5). Because participants were familiar with these simple emotions, the conversation map worked well to collect their experiences. In addition, we had to rely more on observations during the activities and on the information provided by the caregivers.

4 | Discussion

In this study, we aimed to explore the barriers and facilitators of older adults with ID regarding PA using co-design methods. We noted that participants encountered too many barriers to become physically active on their own initiative. Because many personal barriers are difficult to address directly, potential solutions to stimulate PA may initially be found in modifying contextual factors. The most important facilitators were to promote PA together with others, to receive encouragement and compliments and to be offered activities that resonate with personal interests. The modular MakiMove concept demonstrates how these can be designed for a care home context while considering the varying individual abilities and motivations of the residents.

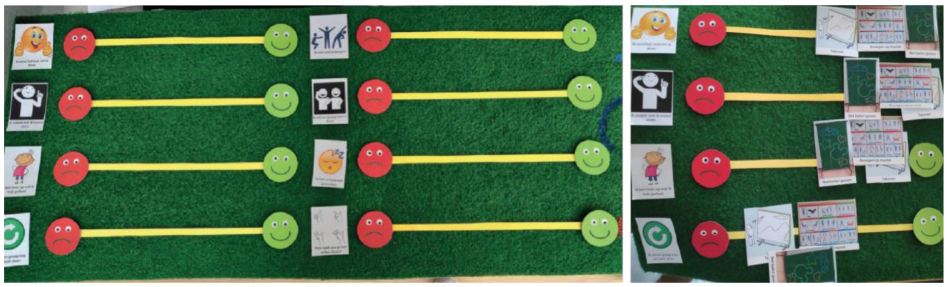

FIGURE 5 | Participants could communicate their experience by placing intervention directions on a scale between a sad and a happy emoticon.

The second aim of this study was to gain insights into how a co-design process can be fitted to older adults with ID. We formulated four lessons learned for co-design that included a prolonged familiarisation period, generative tools and functional prototypes, limited activities with frequent evaluations and a conversational map to communicate through smileys and pictures. Our lessons learned can serve as a starting point for designers and researchers aiming to perform a participatory approach with older adults with ID.

4.1 | Interpretation of Results

Existing literature describes many generic barriers and facilitators to PA (van Schijndel-Speet et al. 2014; Bossink et al. 2017; Salomon et al. 2019; Jacinto et al. 2021), whereas our study provides barriers and facilitators in a specific care home context. Some barriers and facilitators from the literature were reproduced (e.g., lack of time of caregivers and anxiety), yet our participatory approach pointed mostly towards facilitators that reflected the importance of adapting an intervention to the interests and capabilities of the individual residents. Therefore, an intervention should be open and modular, which is in line with conclusions from Westrop et al. (2024) who highlight the complex nature of PA promotion in adults with ID. PA promotion is highly person and context dependent, and we suggest that it should be approached through participatory methods to find out what resonates with target users and their context.

During the project, we established intensive one-to-one contact between each participant and the researcher and were able to adjust our design activities based on user needs, abilities and their context. This approach relates to competency-based co-design, described by Bayor et al. (2021) as an approach to include people with different levels of physical, sensory and cognitive abilities and disabilities to participate equally in design activities. We believe this approach—taking into account the full diversity of the participants in our methods and activities—enriches our insights and builds upon current knowledge and directions for co-designing with people with ID (Birčanin et al. 2021; Sitbon and Farhin 2017). Through our broad scope during the project, we identified barriers and facilitators in relation to capabilities of the users, their physical surroundings and other stakeholders like their caregivers. Although digital interventions provide promising opportunities to promote PA (van Biesen et al. 2023), our bottom-up research-through-design approach led us towards the design of a non-digital and low-cost intervention to enhance independent use and uptake. However, our experiments have also shown the challenges of independent PA as well as the joy of performing activities together with others and receiving encouragement and compliments. Ideally, we would consider the mental well-being of residents to be at least as important as their physical well-being, and we would rather look for 'buddies' than for independent PA (Maenhout and Melville 2024). These insights into barriers and facilitators can help caregivers promote PA in a home setting.

4.2 | Strengths and Limitations

The main strength of our study is that we provide an authentic description of barriers and facilitators for older adults with ID to promote PA in a care home. The prolonged engagement and personal approach in the individual sessions empowered residents to express experiences and opinions. In addition, our creative and responsive research approach forwarded new perspectives on barriers and facilitators and led to original findings. For example, we looked beyond increasing the PA level and in general investigated activities that resonated with them. As a result, our focus was on creating a positive experience for the residents, which may also eliminate the often-present prejudice that PA is a necessary evil.

The relationship that the design researcher built with residents led to credible and authentic findings, yet this also shows that research findings and interventions for older adults with ID largely depend on the relationship that developers and researchers have with their participants. In this study, the design researcher spent considerable time at the care home to build trust and gain familiarity with the residents. This personal attention may have favourably influenced the residents' responses to the activities that were presented to them. Hence, in follow-up research, we will explore if the MakiMove concept is transferable to contexts where limited personal attention is available.

Within the constraints of this study, one design researcher performed most of the analysis. Through a thorough approach with regular member checks, data saturation was achieved, leading to a complete picture of barriers and facilitators. Yet a deeper understanding could be achieved if a socio-behavioural scientist and design researcher together perform and analyse participatory research activities.

5 | Conclusion

This study identified barriers and facilitators that need to be addressed when supporting PA in older adults with ID. Because many personal barriers are difficult to address directly, potential solutions to stimulate PA may initially be found in modifying contextual factors. Insights into these barriers and facilitators can help caregivers promote PA in a home setting. Additionally, due to the wide range in personal interests and capabilities of older adults with ID, modularity of an intervention is crucial. This also applies to the research and development approach, where flexibility and extended effort are required for collaboration with this target group. As a result, our study aids in understanding participatory development of PA interventions for older adults with ID that fit their personal needs and the context they live in.

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Ethics Statement

Ethical approval was obtained from the Human Research Ethics Committee of Delft University of Technology (Approval Number 2126), and an agreement was provided by the participating healthcare organisation.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Data S1:** Supporting Information