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Cost-effectiveness of the Floodlight® MS app in Austria. Unlocking the mystery of costs and outcomes of a digital health application for patients with multiple sclerosis

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Abstract

Objective: Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease affecting 2.9 million people worldwide, often leading to permanent disability. MS patients frequently use eHealth tools due to their relatively young age. The Floodlight® MS app is a scientifically designed smartphone application that helps patients monitor hand motor skills, walking ability and cognition between medical appointments. This study assesses the cost-effectiveness of using the Floodlight® MS app alongside standard-of-care (SoC) versus SoC alone in patients with relapsing-remitting MS (RRMS) from the perspective of the healthcare system.

Methods: A 10-year decision-analytic model was developed to assess the cost-effectiveness of incorporating the Floodlight® MS app alongside SoC. The analysis included treatment-naive individuals and those already on drug therapy, modelling the app's role in early detection of disease progression and relapses to improve quality-of-life.

Results: For treatment-naive patients, using the Floodlight® MS app resulted in a 2,660 € increase in total costs but yielded potential medical-cost savings of 786 € through health improvements. These patients experienced fewer relapses and slower disability progression, translating to a quality-of-life improvement of 4.5 months in perfect health and an incremental-cost-effectiveness-ratio (ICER) of 7,071 €. Pre-treated patients showed similar trends, with medical-cost savings of 718 €, an ICER of 7,864 €, and a quality-of-life improvement of 4.2 months. Higher effectiveness (+5%) led to an additional 8.3 months in perfect health and a reduction in overall costs.

Conclusion: The analysis demonstrates that the Floodlight® MS app is a cost-effective digital health application, encouraging broader discussions on maximizing the potential of software-as-medical-devices within the care pathway.

Keywords

Cost-effectiveness, cost-utility, multiple sclerosis, digital health application, Floodlight® MS

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Introduction

Globally, approximately 2.9 million individuals are currently affected by multiple sclerosis (MS),[1] with a rising prevalence among children and adolescents.[2] In Austria, the incidence of MS is approximately 19.5 per 100,000 individuals, with a nationwide prevalence estimated at around 159 per 100,000 people,[3] equating to roughly 14,470 patients. Overall, 68.48% of these cases exhibit relapsing-remitting MS (RRMS).[4]

With the advent of smartphones, tablets and wearables, health apps have become part of everyday life for more and more people. Apps can sensitize, educate and help to link health data to one's own behaviors and critically reflect on them. As a result, patients are better informed. This, in turn, has positive effects on the doctor–patient relationship, adherence to therapy and satisfaction.[5,6] In science, this is referred to as participatory decision-making. People with MS are among the patients with a high affinity for digital or online tools.[7] Individuals diagnosed with MS demonstrate a notable inclination towards seeking online resources pertaining to their condition, surpassing the engagement levels observed among individuals with other neurological disorders.[8–10] Moreover, a substantial number of MS patients actively utilize digital platforms for managing their condition, whether by exchanging medical data with healthcare professionals or by employing digital tools to facilitate and sustain beneficial lifestyle adjustments.[8,11,12]

The Floodlight® MS App is a science-based smartphone application that helps MS patients track their hand motor skills, walking ability and cognition between doctor visits. The Floodlight® MS app consists of five individual tests that correlate with the common functional tests (9-hole peg test (9HPT), timed 25-foot walk (T25FW) and symbol digit modalities test (SDMT)).[13] These five tests are CE registered as software as medical device (SaMD) according to EU 2017/745 MDR[14] and have been extensively researched and validated scientifically.[6,13,15–21] The data collected by the tests show the development of motor skills and cognition of MS patients over time and can support individual therapy management in doctor–patient discussions.[18] The Floodlight® MS app thus meets the high quality and security standards for market access in the EU (see Figure 1).[22]

These kinds of digital health applications are a valuable complement to medical care and should play a key role in the digitization of healthcare systems. These interventions hold considerable potential to enhance the safety, effectiveness, and quality of care while also reducing resource consumption and, consequently, healthcare costs. However, despite these promising benefits, there is still limited evidence on the cost-effectiveness of digital tools. This analysis aims to serve as a pilot project to evaluate the feasibility of conducting a cost-utility analysis, the gold standard for assessing innovative health interventions, for a digital health application, since this type of evaluation also serves as a basis for decision-making by the payers.

The aim of this health economic study is to evaluate the cost-effectiveness of the use of the Floodlight® MS app plus standard-of-care (SoC) versus no use (SoC alone) in patients with RRMS from the perspective of the Austrian healthcare system.

Methods

In order to evaluate the added value of the Floodlight® MS app, it was necessary to map out patient journeys within the SoC framework. A Markov cohort model was constructed, drawing from two relevant published models. These models were chosen for their ability to account for treatment switches and accurately represent real-world clinical scenarios. One of the selected models is a study evaluating the MS Sherpa app,[23] while the other is an Austrian cost-effectiveness assessment.[24]

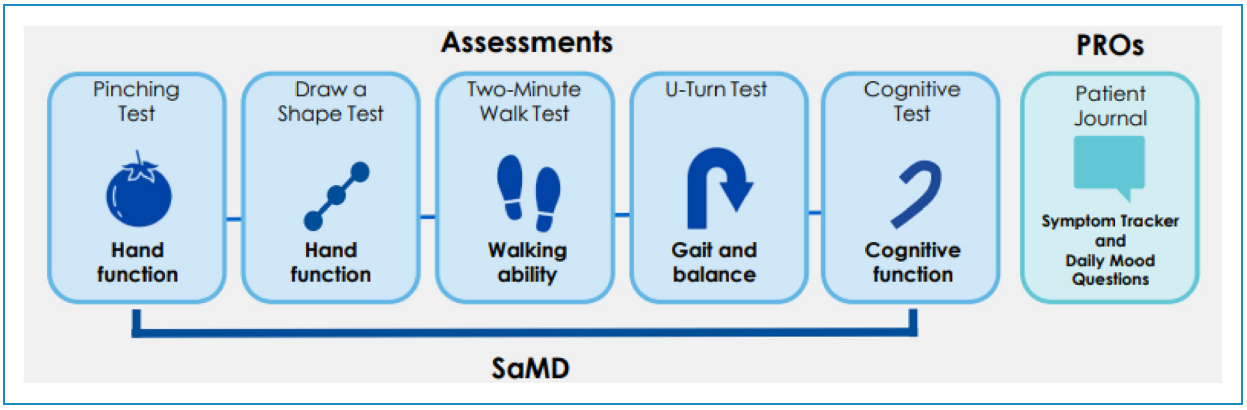

Figure 1. Overview of the five tests in the three domains of the Floodlight® MS app. Floodlight MS is a digital solution for remote assessments in multiple sclerosis (MS) for use in clinical practice, comprising five software as a medical device (SaMD) assessment and a Patient Journal.[41]

Table 1. Overview of immunotherapies by disease activity.

Category 1	Category 2	Category 3
• Dimethylfumarat	• Cladribin	• Alemtuzumab
• Glatiramerazetat	• Fingolimod	• Natalizumab
• Interferon beta	• Ozanimod	• Oceliztumab
• Teriflunomid	• Ponesimod	• Ofatumumab

Source: German Society of Neurology (2023).[25]

The model assumes that MS patients in both comparison groups receive SoC therapy. The SoC therapy, including disease modifying treatments (DMTs) according to the recommendations outlined in the guidelines of the German Society of Neurology (2023) (refer to Table 1).[25] Treatment decisions are differentiated based on the severity of the condition, categorized as mild/moderate or (highly) active forms of MS, for which various treatment options are available. The current model analyzed two cohorts of patients with RRMS: treatment-naive patients starting treatment and pre-treated patients.

The treatment sequences for the treatment-naive patient population comprise the following SoC therapy:

- No therapy > DMTs of category 1 > DMTs of category 2 > DMTs of category 3 (Base case)
- No therapy > DMTs of category 2 > DMTs of category 3
- No therapy > DMTs of category 3

The treatment sequences for the pre-treated patient population comprise the following SoC therapy:

- DMTs of category 1 > DMTs of category 2 > DMTs of category 3 (Base case)
- DMTs of category 1 > DMTs of category 3
- DMTs of category 2 > DMTs of category 3

Both cohorts were initially proportionally assigned to 11 EDSS states (EDSS 0, EDSS 1, EDSS 2, EDSS 3, EDSS 4, EDSS 5, EDSS 6, EDSS 6.5, EDSS 7, EDSS 8 and EDSS 9) when entered the model. It is assumed that the therapy-naive patients are distributed to a large extent in the stages EDSS 0, EDSS 1 and EDSS 2 and EDSS 3. The distribution of pre-treated patients corresponds to the Austrian MS patient characteristic (see section "Simulated cohort"). Using EDSS health states allow to distinguish among DMTs regarding disability progression, relapse rate, treatment discontinuation, costs and quality of life. Due to the short Markov cycles of 3 months, patients can only worsen or improve by one EDSS stage in the next cycle. Over time, patients pass between these states based on a set of transition probabilities.

In treatment-naive patients, disease progression prompts the initiation of therapy, for example a drug from category 1. Subsequently, if the EDSS continues to deteriorate, a therapy switch to a higher-category drug, for example from category 2, is implemented. At model start, the pre-treated cohort is initially on first-line therapy, that can be either a category 1 or category 2 drug. In case of EDSS deterioration, a switch to a higher-category drug, like category 2 drugs, is done. Some patients discontinue therapy and do not switch to any therapy. Adverse events represent a tunnel state leading to a therapy switch within the category. The incidence of a relapse is therapy-dependent, causes costs and reduces quality of life (disutility) at the time of onset. The RRMS can develop into an SPMS. Patients can die from any health condition. Once death state (EDSS = 10) is reached it remains for the duration of the simulation (Figure 2).

The following health states were defined:

- 11 health states based on EDSS scores regarding disability progression based on EDSS scores
- 4 health states described the treatment sequences (category 1–3) including no treatment.
- 1 health stage considered relapses.
- Adverse events were summarized in one cumulated health state (tunnel state) (Table S4)
- Death

Costs were calculated for each cycle in Euros. The model provides cumulative costs, outcomes expressed as EDSS at the endpoint, relapses avoided, and quality-adjusted life years (QALYs). Additionally, it calculates the incremental cost-effectiveness ratio (ICER), a combined measure, by dividing the cost difference between two interventions by the difference in their effects.[26] It is usually the main result of an economic evaluation. The ICER can be estimated as:

$$\mathrm{ICER} = \frac{(C_1 - C_2)}{(E_1 - E_2)} = \frac{\Delta C}{\Delta E}$$

where C_1 and E_1 are the cost and effect in the intervention group and where C_2 and E_2 are the cost and effect in the control group. It provides information on extra cost associated with one extra unit of health effect.[26]

In Austria, an explicit ICER threshold has not been implemented. However, in an international context, it's commonly assumed that a value below 25,000 € is deemed cost-effective. Based on this defined willingness-to-pay (WTP) threshold the net monetary benefit (NMB) provides a breakdown of how costs and effects contribute to the monetary value of using the Floodlight® MS app instead of no application, which represents the value of an intervention in monetary terms.[27]

$$\mathrm{NMB} = (\Delta E * \mathrm{WTP}) - \Delta C$$

The NMB is positive if the ICER is below the WTP-threshold of a quality-adjusted life-year.

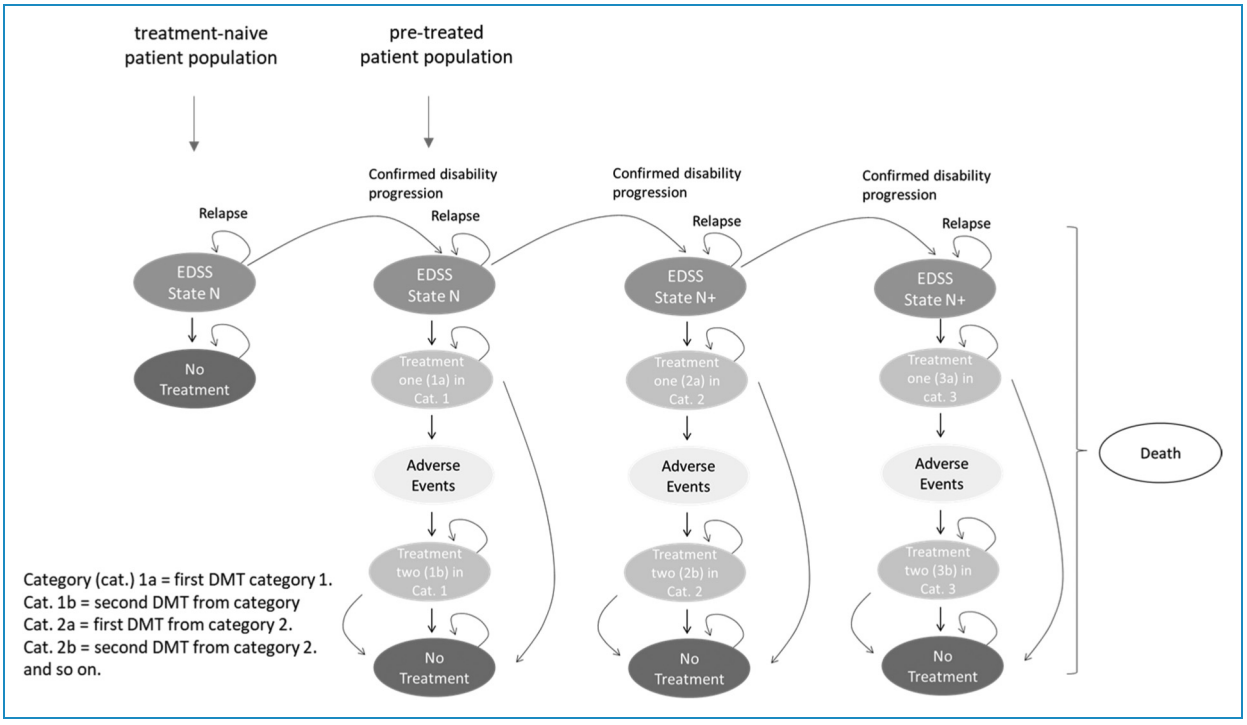

Figure 2. Markov model. Markov process with cycle length of 3 month and 18 defined states. Disease progression is represented using EDSS health conditions. These include the following 11 stages: EDSS 0, EDSS 1, EDSS 2, EDSS 3, EDSS 4, EDSS 5, EDSS 6, EDSS 6.5, EDSS 7, EDSS 8 and EDSS 9. The health condition relapse causes costs and reduces the quality of life (disutilty) at the time of onset. Disease progression leads to initiation of therapy and subsequently to a therapy switch to the next category. Adverse events result in a therapy switch within the category. Some patients discontinue therapy and do not switch to any therapy. The RRMS can develop into an SPMS. Patients can die from any health condition.

A 10-year time horizon was selected to ensure that all significant and relevant outcomes are captured. To address uncertainty and to assess the robustness of our findings, we carried out deterministic and probabilistic sensitivity analyses.

The model was constructed and analyzed using Microsoft Excel 365 (Version 16.77.1, Redmond, WA, USA). The analysis was conducted in consideration of the Modelling Good Research Practices published by the ISPOR Task Force[28] and the Austrian health economic guidelines.[29]

All data utilized in this study are sourced exclusively from published literature. The model incorporates necessary assumptions, which were formulated based on the expert opinions of the author group. The use of Floodlight® MS app for this study was approved by Roche.

Simulated cohort

The Floodlight® MS app is not limited to a specific MS target group. However, it still seems realistic that not all patients can benefit equally from the use of the Floodlight® MS app. The use of the Floodlight® MS app in patients with high stages of EDSS (EDSS 6–9) may be considered rather unlikely. For the economic model, therefore, the target population was defined as patients with RRMS with an EDSS below or equal 5.

A real-world evidence (RWE) study pertinent to treatment-naïve MS patients was identified from the literature and used to inform the EDSS distribution in the first model cycle. This retrospective longitudinal observational study, known as CLARENCE, examined a substantial cohort of over 1900 patients with RRMS in England who were treated with cladribine.[30] At the initiation of treatment with cladribine, the median baseline EDSS score was 2.5, ranging from 0 to 8.5. Notably, 1108 patients (57%) had an initial EDSS score below 3.0, while 418 patients (22%) had a score of 5.0 or higher.[30] These data, covering EDSS stages 0 to 5, were utilized in the economic model for the EDSS distribution. The starting age in the model was set at 35 years.

The distribution of EDSS scores among pre-treated patients is derived from a cost-of-illness analysis conducted as part of a Europe-wide study on the expenses associated with MS.[31] This analysis draws upon data from MS patients in Austria. Similar to the approach taken with treatment-naive patients, the EDSS scores ranging from stages 0 to 5 were utilized for establishing the baseline distribution and were standardized to 100%. The model's initial age parameter was defined as 40 years.

Clinical, cost and utility data inputs

The integration of the Floodlight® MS app and its impact on treatment decisions were implemented within the economic evaluation. Given the absence of documented real-world effectiveness of the Floodlight® MS app in clinical routine, it is presumed that its utilization provides patients and their neurologists with earlier insights according disease activity. Consequently, this may prompt earlier transitions to subsequent treatments compared to scenarios without Floodlight® MS app. Second-line treatments are generally recognized for their enhanced efficacy albeit at higher costs. Prompt transitions to these treatments facilitated by the Floodlight® MS app may mitigate disease progression and MS exacerbations, potentially resulting in improved health outcomes, quality of life, and anticipated cost savings.

Therefore, the effectiveness of the Floodlight® MS app can be summed up as follows:

- Percentage of patients with early detection of disease progression as well as MS relapses
- Percentage of patients with an improved quality of life

In the base case assumption, an effectiveness of the Floodlight® MS app of 5% was selected. In addition, an effectiveness up to 10% has been identified as plausible by Cloosterman et al.[23] and clinical experts and authors of this publication.

The Floodlight® MS app has shown that 70% adherence can be achieved in a 24-week study.[6] In a shorter period of 3 months, an adherence of >90%, in the case of MS-Sherpa, could even be shown.[23] These values are consistent with the high adherence of other digital biomarker-based eHealth interventions such as MSCopilot, which shows that 85% of patients surveyed are willing to use the intervention more than once a month.[23] Based on the observed data, the model was assumed to have an adherence of 70% after 2 years. Applying the time adjustment again, there is an adherence rate of 91% after 1 year, 38% after 5 years and 21% after 10 years (see Figure S1).

The transition probabilities required for the model, delineating shifts between health states, were established through a focused literature review. The clinical dataset encompasses the rates of progression and relapse, progression to secondary progressive multiple sclerosis (SPMS), treatment discontinuation, AEs and death. In this context, input data of a previously published economic model for Austria[24] were updated and incorporated within this framework. All clinical data are described and presented in detail in Supplementary Appendix (Chapter S1 Transition probabilities and clinical input data).

The cost assessment relied on attributing costs to various health states. Costs associated with each health state were determined based on the utilization of resources linked to that state. This resource usage, encompassing the type and frequency of medical goods and services provided to the patient, along with their monetary value (comprising prices, tariffs, and/or opportunity costs per unit of medical goods and services), was employed to compute the total direct costs within the Austrian context. When estimating the costs of RRMS in Austria, only direct medical expenses were considered in the analysis. These encompassed the Floodlight® MS app costs, medication costs plus application, monitoring costs, relapse costs, EDSS stage costs and AE costs. Direct medical costs were gathered from the payer's perspective for the year 2023. To account for time preference, as a time horizon of 10 years was used, a discount rate of 5% per year was applied.[29] A detailed description of the costs can be found in Supplementary Appendix (Chapter S2 Cost assessment).

Utilities reflect a measure of preference for different health states, where preference corresponds to the perceived value or desirability of each state. The utilities for the health states included in the model were derived from international literature and, when necessary, adjusted to a 0-to-1 utility scale, with 0 representing death and 1 representing perfect health, using weighting factors. The concept of QALYs allows for the combination of both the quantity and quality of life years impacted by health interventions into a single metric. QALYs were calculated by multiplying the time spent in each health state by its corresponding utility score.[32] The analysis incorporates utility weights for different EDSS states and disutilities associated with MS relapse and AEs. Comprehensive details can be found in Supplementary Appendix (Chapter S3 Health state utilities).

Sensitivity analysis

A deterministic one-way sensitivity analysis was performed to assess how changes in individual input parameters affect the model's outcomes, particularly the incremental cost-effectiveness ratio (ICER), thereby evaluating the robustness of our results. Where available, input ranges for the sensitivity analysis were derived from 95% confidence intervals (CIs). In cases where CI data were not available (e.g. for costs), input ranges were established by adjusting percentage values up or down from the baseline estimates. Additionally, a probabilistic sensitivity analysis was performed. This comprehensive probabilistic sensitivity analysis enables an examination of each parameter's contribution to model outcomes, while considering the uncertainty of other model parameters. To achieve this, we integrated a probability distribution of the input variables using a second-order Monte Carlo simulation. Each simulation drew a different value randomly from the distribution of each variable. Second-order Monte Carlo simulations were conducted for 1000 hypothetical patients based on the distributions of all input variables, utilizing gamma distribution for costs and beta distribution for probabilities and utilities.

Results

Treatment naive MS patients

The average total cost per patient in the SoC plus Floodlight® MS group amounts to 92,935 € over a 10-year period, following a treatment pathway starting from no therapy to a DMT of category 1, then category 2, and finally category 3 ("base case"). Conversely, the average patient in the comparison group, receiving only SoC without the Floodlight® MS app, accrued an average total cost of 90,275.28 € over the same duration. When considering solely costs, there is a cost disparity of 2,660.03 € for SoC plus the Floodlight® MS app compared to SoC alone. However, overall, the utilization of the Floodlight® MS app resulted in a reduction of medical costs by 786 €.

The findings indicate that adopting the combination of SoC along with the Floodlight® MS app correlates with an enhancement in QALY, specifically 0.3762 QALYs or 4.51 months in perfect health, if a QALY corresponds to one year in perfect health. This translates to an ICER of 7,071.49 € (refer to Table 2). Applying a "willingness-to-pay" threshold of 25,000 €, the NMB totals 6,744.04 €.

Over the span of 10 years, the utilization of the Floodlight® MS app leads to reduced disease progression. With an average baseline EDSS of 1.99, the average EDSS after a decade in the Floodlight® MS app group stands at 3.29, compared to 3.59 without the Floodlight® MS app (refer to Figure 3(a)). Furthermore, the implementation of the Floodlight® MS app results in a decrease of 0.86 MS relapses over the same 10-year period.

An increased effectiveness (10%) of the Floodlight® MS app leads to a further decrease in overall costs compared to the base case. This translates to a gain of 8.9 months in perfect health. Consequently, the ICER decreases to 2103 € (refer to Supplementary Appendix Table S5).

Initiating therapy at a higher category along with the utilization of the Floodlight® MS app results in a higher ICER compared to the base case. For instance, if patients start treatment with a category 2 product, the ICER amounts to 7406 €. However, if a category 3 drug is prescribed, the ICER increases to 7488 € (refer to Supplementary Appendix Table S5).

Pre-treated MS patients

Among patients previously treated, the use of the Floodlight® MS app alongside SoC once again leads to higher costs, amounting to 2,727.72 € more compared to SoC alone (148,603.73 € vs. 145,876.01 €). However, the reduction in medical expenses was by 718 €. The combination of SoC with the Floodlight® MS app resulted in an improvement of 0.3469 QALYs, equivalent to 4.16 months in perfect health. Consequently, this yields an ICER of 7,863.77 € (refer to Table 2).

Over the horizon of 10 years, the utilization of the Floodlight® MS app leads to reduced disease progression. With an average baseline EDSS of 2.36, the average EDSS in the Floodlight® MS app group decreases to 3.27 compared to 3.54 at model endpoint (refer to Figure S3b). Furthermore, the implementation of the Floodlight® MS app results in a reduction of 0.35 MS relapses over the same 10-year period.

With a higher effect (10%) of the Floodlight® MS app, there is a reduction in overall costs compared to the base case. This improvement can lead to a gain of 8.3 months in perfect health. Consequently, the ICER decreases to 2,946 € (refer to Supplementary Appendix Table S6).

Transitioning therapy from category 1 to category 3 alongside the use of the Floodlight® MS app results in an increase in the ICER to 8,036 € compared to the base case. Similarly, shifting therapy from category 2 to category 3 yields an ICER of 8,055 € (refer to Supplementary Appendix Table S6).

Deterministic sensitivity analysis

A one-way sensitivity analysis evaluating the effects of variations in individual parameter assumptions on ICER are shown in Figure 4.

In treatment-naïve patients, the adherence rate variations exert the most significant influence, trailed by the discount rates of utilities and costs, the placebo ARR and the inpatient MS relapse costs. The ICER spans from 6,160.69 € to 8,060.50 €.

In pre-treated patients, variations in the adherence rate exhibit the most pronounced impact, followed by the discount rates of utilities and costs, the utility value for EDSS 2 and 1, and health state costs for EDSS 5. The ICER spans from 6,876.05 € to 8,936.29 €

Probabilistic sensitivity analysis

The ICER scatter plot, representing incremental costs on the *y*-axis and incremental QALYs on the *x*-axis, portrays the cost-utility analysis outcomes within the treatment-naive MS patient group. It reveals that SoC plus the Floodlight® MS app compared to SoC is costlier, yet more effective when expressed in QALYs, all points are clustered in the upper right quadrant (refer to Figure 5(a)). The average incremental cost amounts to 2,849.76 €, while the incremental QALYs reach 0.385. This yields a probabilistic ICER of 7,396.93 €.

The acceptability curve indicates that when considering a WTP threshold of 25,000 € per QALY gained, the Floodlight® MS app plus SoC versus SoC is deemed cost-effective in 100% of instances. Even with a WTP of 10,000 €, 93.9% of all simulations are in the cost-effective range.

The findings from the pre-treated patient population reveal that SoC plus the Floodlight® MS app, compared

Table 2. Cost-effectiveness results.

Results for the treatment naive patients		
Cost components	SoC plus Floodlight® MS	SoC
Floodlight® MS-App costs	3,445.78 €	
Medication costs plus application	27,767.50 €	27,339.33 €
Monitoring costs	4,151.57 €	4,169.52 €
Relapse costs	1,789.08 €	1,816.18 €
EDSS stage costs	49,110.14 €	49,596.41 €
AE costs	6,671.25 €	7,353.82 €
TOTAL costs	92,935.31 €	90,275.28 €
95% CI total costs	88,709–97,271	85,835–95,042
Cost difference	2,660.03 €	
QALYs		
QALYs	6.3072	5.9311
95% CI QALYs	6,057–6,600	5,621–6,200
QALY difference	0.3762	
ICER/QALY	7,071.49 €	
Clinical outcomes		
Mean EDSS Baseline	1.99	1.99
Mean EDSS Endpoint	3.29	3.59
Number of MS relapses	8.39	9.25
Results for pre-treated patients		
Cost components	SoC plus Floodlight® MS	SoC
Floodlight® MS-App costs	3,445.78 €	
Medication costs plus application	80,608.65 €	80,676.95 €
Monitoring costs	8,482.86 €	8,482.18 €
Relapse costs	2,382.00 €	2,381.98 €
EDSS stage costs	50,994.78 €	51,363.12 €
AE costs	2,689.66 €	2,971.78 €

(continued)

Table 2. Continued.

Results for pre-treated patients		
Cost components	SoC plus Floodlight® MS	SoC
TOTAL costs	148,603.73 €	145,876.01 €
95% CI total costs	141,146–155,971	138,156–153,692
Cost difference	2,727.72 €	
QALYs		
QALYs	6.1942	5.8474
95% CI QALYs	5.884–6.434	5.533–6.088
QALY difference	0.3469	
ICER/QALY	7,863.77 €	
Clinical outcomes		
Mean EDSS Baseline	2.36	2.36
Mean EDSS Endpoint	3.27	3.54
Number of MS relapses	3.34	3.69

to SoC alone, emerges as more costly but also more effective in 100% of simulations. The average incremental cost stands at 2,936.74 €, while the incremental QALYs amount to 0.355. The resultant probabilistic ICER from 1000 iterations is 8,265.35 €. In the simulation model, SoC plus the Floodlight® MS app versus SoC proves to be cost-effective in 100% of all cases. With a WTP of 10,000 €, 84.3% of all simulations would be cost-effective (refer to Figure 5(b)).

These probabilistic findings validate the outcomes obtained from the deterministic base case analysis.

Discussion

This study evaluated the cost-effectiveness of integrating the Floodlight® MS app into SoC in patients with RRMS over a 10-year period. The findings show that using the Floodlight® MS app results in reduced costs of illness (ranging from −718 € to −786 €) and improved EDSS scores over 10 years. Even with a conservative assumption of 5% effectiveness, the app still achieves cost savings. With a higher effectiveness of 10%, the medical cost savings increase to 1,407 € and 1878 €, respectively. The benefits are most pronounced in treatment-naive patients (with an average EDSS difference between groups ranging from −0.29 to −0.39), but pre-treated patients also experience significant benefits (with an average EDSS difference ranging from −0.27 to −0.35). Moreover, the Floodlight® MS app users experience fewer MS relapses, averaging between −0.86 and −1.68 in treatment-naive patients and between −0.35 and −0.68 in pre-treated patients over the 10-year period. The calculated ICERs indicate that the Floodlight® MS app is highly cost-effective across all patient groups and efficacy assumptions.

In summary, earlier detection of disease progression and MS relapses, potentially through the use of the Floodlight® MS app, combined with timely therapy adjustments, can help prevent further disease advancement. A European study consistently found that worsening EDSS scores lead to a significant reduction in quality of life.[33] This decline is also associated with increasing costs: 25,100 € at EDSS 0–3, 44,100 € at EDSS 4–6.5 and 73,800 € at EDSS 7–9.[34] In the realm of digital health applications, the primary focus has been on evaluating the effectiveness of telemedicine. However, little is known about the economic impact of telemedicine in chronic neurological diseases like MS. This gap may partly explain the limited adoption and lack of widespread reimbursement for such technologies.[35]

A systematic literature review on telemedicine in chronic neurological diseases, which included home monitoring and assessment devices, demonstrated cost-effectiveness

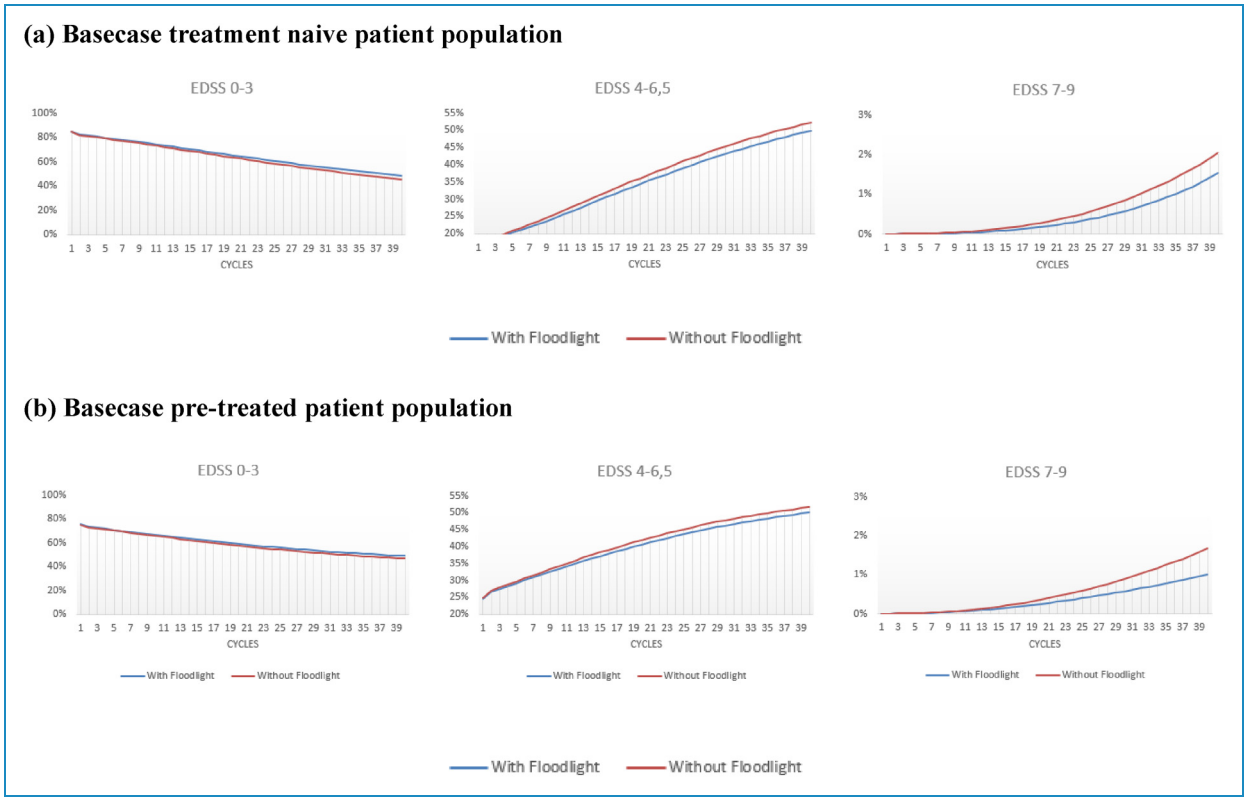

Figure 3. EDSS over the time course of SoC with the Floodlight® MS app vs. SoC without the Floodlight® MS app. (a) Basecase treatment naive patient population; (b) Basecase pre-treated patient population.

based on findings from two extracted studies.[35] One of the two studies, conducted by Cubo et al.,[36] compared the cost-effectiveness of home-based motor monitoring with traditional office-based monitoring over the course of 1 year in patients with advanced idiopathic Parkinson's disease. The calculated ICER focused on functional status, motor impairment, and motor complications, but did not account for QALYs. The cost required to reduce one unit on the UPDRS ranged from 126.72 € to 701.31 €.[36] The second study was an economic evaluation based on the SMART4MD randomized controlled trial, which compared a tablet application for individuals with mild cognitive impairment and their informal caregivers to standard care, aiming to improve or maintain quality of life from a healthcare provider's perspective over a 6-month follow-up period. The results showed no significant differences in costs or QALYs for both patients and caregivers.[37] The strength of this study lies in its use of QALYs and its inclusion of caregiver burden.[35]

Only one cost-effectiveness analysis of an MS app has been identified in the literature. Clostermann et al.[23] conducted a study examining the additional benefits of digital biomarker-based eHealth interventions within the MS treatment pathway, focusing on MS Sherpa as an illustrative example. The analysis adhered to the Dutch guidelines for health economic evaluations. It modelled the effectiveness of MS-Sherpa in early disease detection and treatment adjustment across varying effectiveness rates of 5%, 10%, 15% and 20%. From a societal perspective, MS-Sherpa demonstrates dominance—means both clinically superior and cost saving—at effectiveness rates of 15% and 20%, respectively. Moreover, MS-Sherpa proves to be cost-effective in scenarios with effectiveness rates of 5% and 10%, with ICERs of 14,535 € and 4,069 €, respectively.

The findings from Clostermann et al.[23] align with our analysis. With an efficacy increase to 15%, a dominant outcome would be attained in treatment-naive patients. In the pre-treated patient group, the ICER decreases to 1,303 € at 15% effectiveness and to 487 € at 20%.

In their study, Marrie et al.[11] surveyed 6423 MS patients, determining that the utilization of eHealth technologies is widespread within the MS community, aiding in the exchange of healthcare information with providers. The utilization of mHealth apps is perceived to offer health benefits. Nonetheless, the adoption of eHealth and mHealth technologies exhibits significant variations influenced by sociodemographic factors. It's imperative for healthcare providers to recognize these disparities, particularly as these technologies become more prevalent in healthcare settings.

The current cost-utility analysis is based on the premise that it meets the methodological standards applied to other

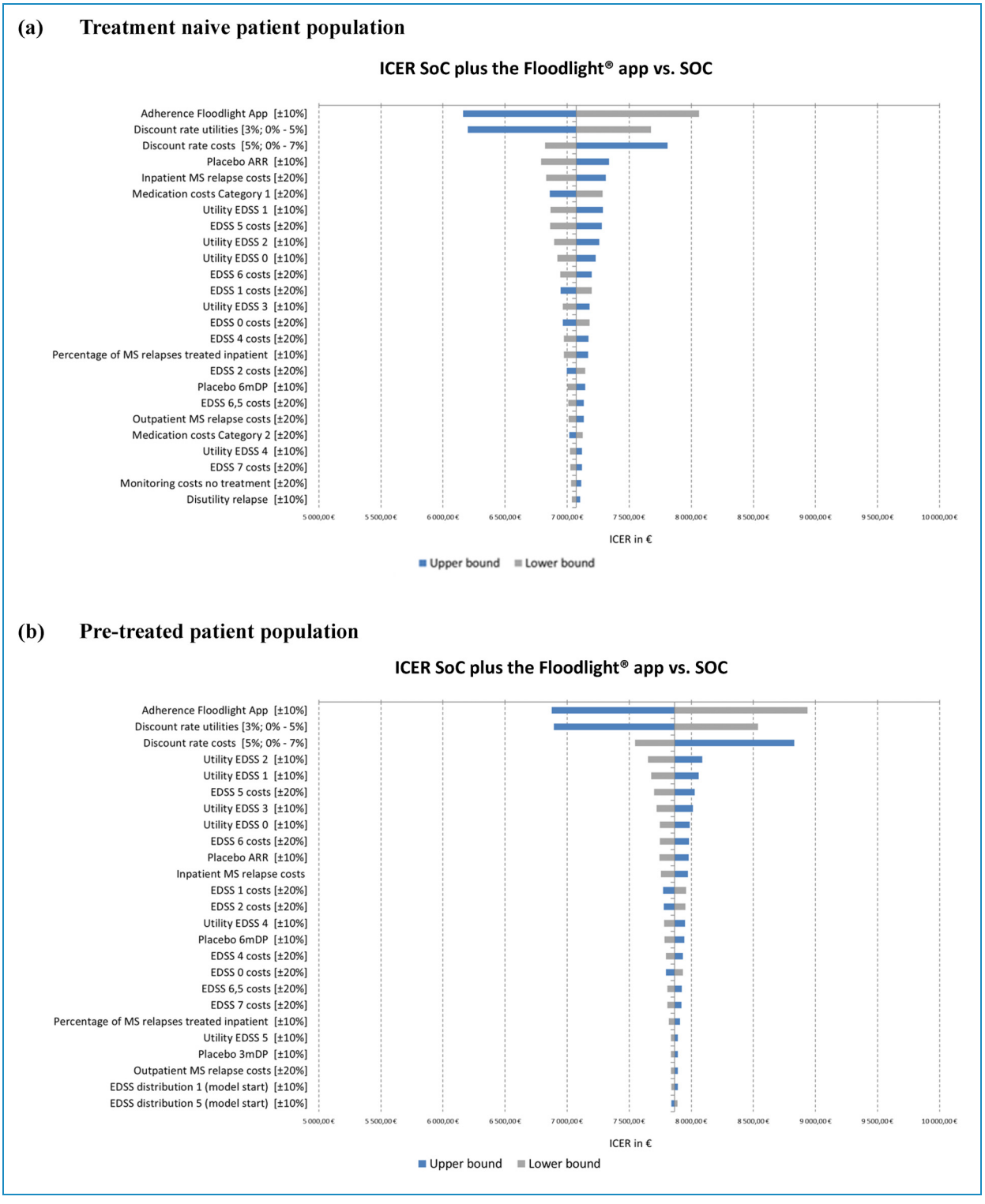

Figure 4. Deterministic one-way sensitivity analysis visualized as tornado plots. Deterministic sensitivity analysis was used to identify the critical variables affecting risk analysis. Results are displayed as tornado diagrams for the 25 variations with the greatest impact, where each bar represents a one-way sensitivity analysis, and width of bars represents impact on model results. The ICER is plotted on the *x*-axis. (a) Treatment naive patient population; (b) pre-treated patient population.

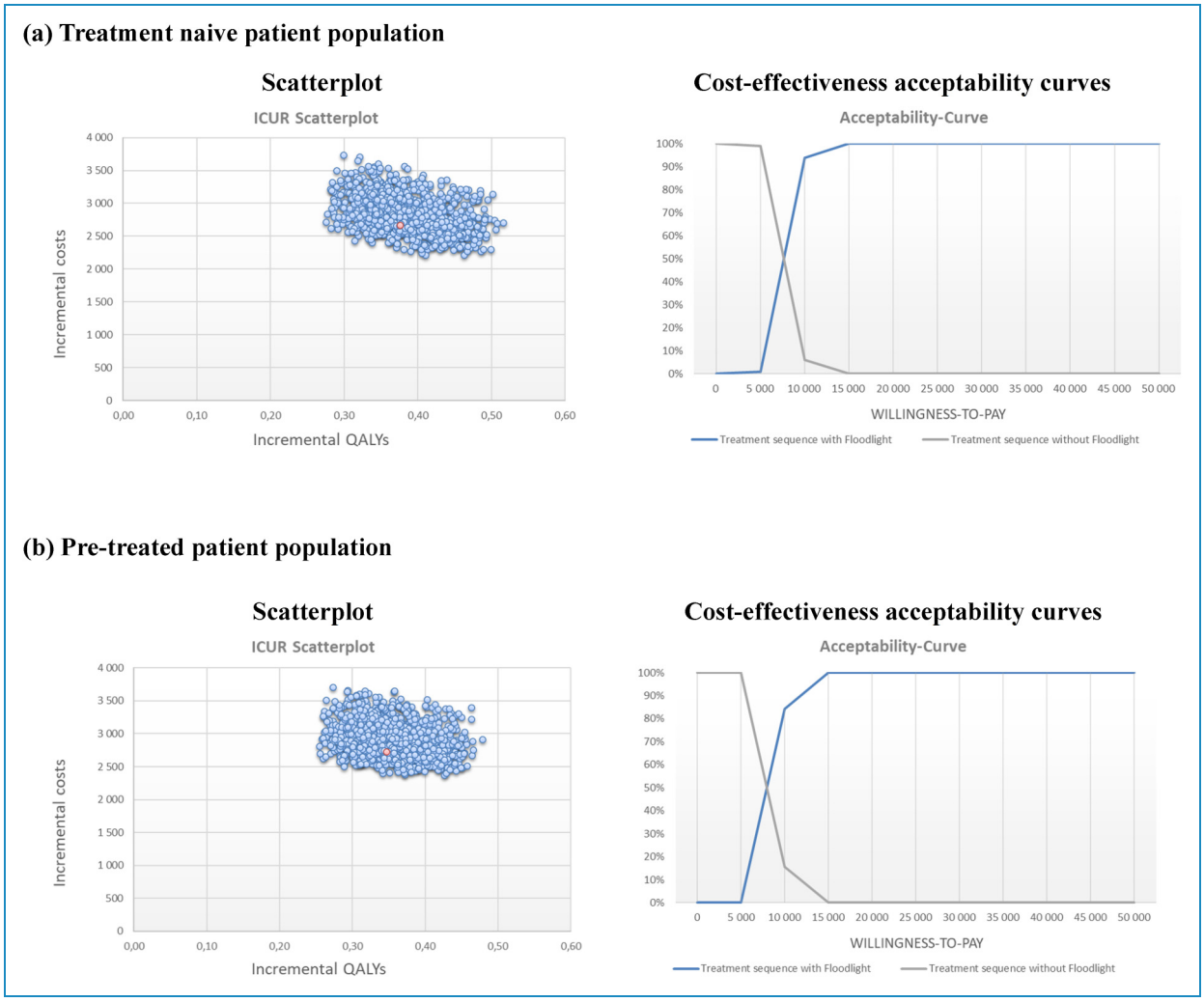

Figure 5. Probabilistic sensitivity analysis: the scatterplot shows results of the Monte Carlo probabilistic sensitivity analysis for 1000 patients. Incremental cost is plotted on the *Y*-axis, incremental effectiveness is plotted on the *X*-axis. Cost-effectiveness acceptability curves display the percentage of iterations that favor teduglutide in comparison with no teduglutide, over a range of willingness-to-pay. The *X*-axis displays reported values as € per QALY. (a) Treatment naive patient population; (b) pre-treated patient population.

healthcare innovations, making it a suitable foundation for reimbursement decision-making. However, the literature shows that most of the evaluations reviewed do not fully align with standard evaluation techniques, and significant improvements are needed before decision-makers can rely on them to provide valid and reliable cost-effectiveness data.[38]

The main strength of our model lies in its comparison of treatment sequences, mirroring real-world clinical practices. By considering successive treatment options and costs, including those after discontinuation of a DMT, we capture the complexities of actual patient management. This approach is substantial for accurately quantifying the benefits of an app used alongside SoC. Notably, existing models for MS drugs typically overlook treatment switches, focusing instead on transitions to no treatment. Our model provides a more realistic depiction of costs and outcomes by aligning with patient pathways. Additionally, it builds upon a published NMA by Samjoo et al.[39] due to the absence of head-to-head RCTs for all SoC treatments. Our model integrates resource utilization data reflective of Austrian clinical practices and reimbursement regulations, eliminating the need for estimations by utilizing 2023 prices and tariffs.

However, there are limitations, such as the lack of clinical trial data for the Floodlight® MS app's effect on disability progression. The current literature lacks assessments of the effectiveness of MS apps or digital health applications, so expert assessments were relied upon for integration into the model. A conservative estimate of 5% effectiveness was used as base case, with up to 10% considered plausible. Higher values were rejected, but re-evaluation could provide clarity. Sensitivity analyses were conducted on disease progression and relapse rates. It's important to note that RCTs included in the NMA may not fully apply

to real-world situations. Discontinuation rates in RCTs in the NMA may not fully reflect routine practice. This could potentially amplify the positive effect of the Floodlight® MS app. Indirect costs associated with MS, such as loss of income, reduced productivity, caregiver burden and diminished quality of life, were not considered in this study due to limited data availability. However, MS imposes a significant economic burden, particularly in terms of employment, with fewer than 20% of patients of working age remaining employed at higher disability levels (EDSS 6.0–8.0).[40] Integrating such indirect costs into the analysis presents challenges due to data scarcity.

Overall, the analysis highlights the cost-effectiveness of the Floodlight® MS app and the increasing self-management among MS patients. Across both base case and scenario analyses, the ICERs consistently remain below 10,000 €, indicating high cost-effectiveness. Moreover, there's a notable uptick in the level of self-management among MS patients. Self-management, defined as the ability to largely shape one's personal and professional development independently of external factors, aligns with the bioethical principle of individual autonomy.[7]

Finally, it is important to note that future research is needed to thoroughly evaluate the efficacy of the Floodlight® MS app, ideally through randomized controlled trials or longitudinal studies.

Conclusion

There is limited research on the cost-effectiveness of MS apps, indicating the need for further investigation. However, integrating a software as a medical device (SaMD) like the Floodlight® MS app has been found to result in cost savings and improved EDSS scores. Health care decision makers or payers may consider using these models to inform funding or reimbursement decisions.

Starting with a SaMD early in the treatment journey has shown significant benefits in reducing disease progression and relapses. The integration of the Floodlight® MS app is highly cost-effective for all patient groups. These findings highlight the importance of early adoption and its potential to enhance patient outcomes. Further research is crucial to evaluate the real-world performance of the Floodlight® MS app. Overall, this study encourages a broader discussion on maximizing the potential of SaMDs within the care pathway.

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Ethical statement: There are no human participants in this article and informed consent is not required as we had used published data only. Incorporates necessary assumptions, were formulated based on the expert opinions of the author group. The use of Floodlight® MS app for this study was also approved by Roche.

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