Psoriasis: Targets and Therapy

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ORIGINAL RESEARCH

Analysis of the Reduction in the Duration of Sick Leave for 32,512 Psoriasis Patients Following the Integration of Targeted Therapies for Psoriatic Disease into the Brazilian Healthcare System: a Retrospective Cohort Study

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Purpose: The Brazilian Unified Health System is an interesting model for international healthcare innovation analysis. Covering over 200 million people, this system stands out as one of the largest purchasers of healthcare technologies worldwide. Our goal in this study was to evaluate how targeted therapies reduce the duration of sick leave for psoriasis patients.

Patients and Methods: We conducted a retrospective cohort study within the Brazilian National Institute of Social Security. The primary outcome was the return to work (cessation of sick leave) of patients with psoriasis. Factors such as age, sex, and access to targeted therapies were evaluated using a Cox proportional hazards model.

Results: Over the 25-year period from 1998 to 2023, 32,512 benefits were granted for psoriasis, totalling an expenditure of $577,478,002.15. Public access to psoriatic arthritis (PsA)-targeted therapies decreased the average minimum wage granted to psoriasis patients on sick leave by 22%, and public access to psoriasis-targeted therapies reduced the average wage by 7%. The availability of these therapies was associated with earlier cessation of sick leave in our proportional hazards model (targeted therapies for PsA: hazard ratio (HR) = 1.90, 95% confidence interval (CI) = 1.82–2.00; targeted therapies for psoriasis: HR = 1.63, 95% CI = 1.54–1.70).

Conclusion: This study highlights a remarkable reduction in costs and sick leave duration due to the implementation of therapies for psoriatic disease by the Brazilian Unified Health System, which underscores the importance of considering detailed indirect cost data when evaluating new health technologies for large populations.

Plain Language Summary: Psoriasis is a chronic inflammatory disease affecting more than 60 million people worldwide. The disease is known to affect genetically predisposed individuals after an environmental trigger, sparking a relentless cycle of skin and systemic inflammation. The Brazilian Unified Health System offers an interesting case study for analysing the financial implications of cutting-edge healthcare technologies. Serving over 200 million diverse individuals, it is one of the world's largest single buyers of healthcare technologies. In the CLEAR and FIXTURE trials, compared with ustekinumab and etanercept, secukinumab not only demonstrated superior efficacy but also significantly reduced work impairment for patients and the associated indirect costs of psoriasis from weeks 16 through 52 in the United Kingdom. Although controlled clinical trials have illustrated the positive impacts of effective therapies for psoriasis, there is a considerable gap in real-world data. Our study examines the impact of targeted therapies on reducing the duration of sick leave for psoriasis patients, leveraging extensive big data analysis from the Brazilian National Institute of Social Security system. Our findings revealed a significant reduction in costs and sick leave durations owing to the implementation

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of these therapies for psoriatic disease. This study underscores a remarkable reduction in costs and sick leave duration due to the implementation of therapies for psoriatic disease by the Brazilian Unified Health System. This finding highlights the importance of considering detailed indirect cost data when evaluating new health technologies for large populations.

Keywords: psoriasis, arthritis, psoriatic, costs and cost analysis, health care costs, health expenditures

Introduction

Psoriasis is a chronic inflammatory disease affecting more than 60 million people worldwide.[1–3] Despite ongoing research, the exact cause remains elusive, but the disease is known to affect genetically predisposed individuals after an environmental trigger, sparking a relentless cycle of skin and systemic inflammation.[4]

Today, psoriasis is not just a skin issue but also a systemic disease linked to many other health problems, including metabolic syndrome, heart disease, joint disorders, and depression.[5,6] Its societal impact is profound, with the disease and its related conditions placing a heavy burden on healthcare systems, patients, and society at large. Although effective treatments can alleviate symptoms, the full extent of their impact on indirect healthcare costs remains incompletely understood.[6]

The Brazilian Unified Health System offers an interesting case study for analysing the financial implications of cutting-edge healthcare technologies.[7] Serving over 200 million diverse individuals, it is one of the world's largest single buyers of healthcare technologies. In 2014, Brazil made a landmark decision to provide targeted therapies such as adalimumab, etanercept, and infliximab to all citizens with severe psoriatic arthritis (PsA). Before these incorporations, access to targeted therapies was incipient and not adequately regulated. This initiative has expanded to include other medications, such as certolizumab pegol, secukinumab, and tofacitinib.[8] Similarly, treatments such as adalimumab, secukinumab, ustekinumab, and risankizumab have been available for psoriasis since 2018.[9] Today, the Brazilian Unified Health System offers a broad range of treatments necessary for the control of severe psoriasis free of charge. Following a protocol based on cost-effectiveness analysis, dermatologists working in the private and public sectors can prescribe psoriasis patients treatment modalities ranging from the most classic therapies, including phototherapy, methotrexate and cyclosporine, to antitumour necrosis factor biologics and the most modern options, including interleukin (IL) 17 or 23 blockers.

Our study assessed how access to these targeted therapies influences the duration of sick leave for psoriasis patients covered by the Brazilian National Institute of Social Security. We also sought to measure the resulting decrease in social security expenses following the introduction of these therapies for psoriatic disease.

Materials and Methods

We conducted a retrospective cohort study within the Brazilian National Institute of Social Security. In 2022, Brazil's social security system included 61,857,906 contributors.[10] In January 2024, we accessed the public Federal Comptroller General's portal, Fala Brasil, and requested data on social security benefits granted to beneficiaries diagnosed with psoriasis (International Classification of Diseases, Tenth Revision (ICD-10): L40, L40.0, L40.1, L40.2, L40.3, L40.4, L40.5, L40.8, and L40.9) from 1998 to 2023. These data were classified according to ICD-10 codes, sex, age, municipality of residence, date of granting and termination of the benefit, and value in minimum wages. To access social benefits, patients are referred to a general practitioner or specialist for examination. Patients are then evaluated by occupational health experts, who record the ICD-10 code related to the benefit. We excluded patients with inconsistent data clearly related to issues in data entry, including negative values in social security benefits.

The primary outcome of this study was the return to work (cessation of sick leave) of patients with psoriasis who were contributors to the Brazilian National Institute of Social Security. Factors potentially influencing this outcome were evaluated, primarily age, sex, and status of access to targeted therapies specific to psoriatic disease.

Cost Analysis

In addition to demographic and clinical information, the data acquired included the number of Brazilian minimum wages and the period of sick leave or retirement of each patient. This information made it possible to calculate the total expenses related to psoriasis related to each patient and each event. The costs related to social security were represented in American dollars ($). We considered the 2024 Brazilian minimum wage (R$ 1412) and the commercial dollar exchange rate as of 8 November 2024, which was R$ 5.33 to the dollar.

Analysis of the Impact of Targeted Therapies on Reducing Sick Leave Duration

We identified targeted therapies as any on-label medication for PsA or psoriasis that had been incorporated into the public Brazilian Unified Health System for PsA or psoriasis itself. To analyse the impact of incorporating these targeted therapies for psoriasis, we compared two major time points. First, we compared patients who began their sick leave before or after 2014, when the national incorporation protocol for PsA was published. Second, we compared patients who began their sick leave before or after 2018, when the protocol for psoriasis was published. For these evaluations, we considered a maximum follow-up period of 10 years for PsA-specific interventions and 5 years for psoriasis-specific interventions.

In this analysis, we included only patients who had either ceased sick leave benefits due to disease control (considered a positive outcome) or those who had transitioned to extended or permanent disability benefits (considered a negative outcome). Finally, we assessed the effects of both PsA and psoriasis-specific interventions by excluding all patients who had commenced sick leave benefits prior to 2015, the year in which the protocols for targeted therapies for PsA were first included in the national Brazilian Unified Health System.

The validity of this model was previously demonstrated during the incorporation of adalimumab for hidradenitis suppurativa, establishing it as a reliable metric for assessing the cost-reduction impact of targeted therapies.[10] This reliability is attributed to the constant increase in the number of contributors to the Brazilian National Institute of Social Security, which consequently raises costs associated with benefits, and the significant annual increase in the use of targeted therapies in Brazil. Any substantial reduction in social benefit costs is therefore unexpected unless it results from a comprehensive national policy, such as the widespread incorporation of effective targeted therapies.

Statistical Analysis

Absolute and relative frequencies were calculated for categorical variables, whereas means and standard deviations (SDs) were used for continuous variables. The annual average minimum wage received monthly by psoriasis patients at the beginning of the benefit in Brazil from 1998 to 2023 was analysed. Regression analysis identified factors associated with the minimum wage granted using the following predictors that were considered relevant: age, sex, region of residence, access to PsA-targeted therapies (pre-2015: "no", post-2014: "yes"), and access to psoriasis-targeted therapies (pre-2019: "no", post-2018: "yes"). An adjusted generalised linear model (GLM) with a log link function and gamma family was applied due to nonnormal outcomes. The results were exponentiated and represented as average ratios (AR).

To assess the effect of access to targeted therapies on the return to work (cessation of sick leave), Log rank tests and Kaplan–Meier survival analyses were conducted. Hazard ratios (HRs) were subsequently determined via an adjusted Cox proportional hazards model using the following predictors that were considered relevant: age, sex, access to PsA-targeted therapies (pre-2014: "no", post-2014: "yes"), and access to psoriasis-targeted therapies (pre-2019: "no", post-2018: "yes"). Proportionality was tested via Schoenfeld residuals, supported by visual inspection of log–log plots.

Statistical significance was set with a p value <0.05 and a 95% confidence interval (CI). Statistical analysis was performed via the survival and survminer packages in R version 4.4.2 (R Core Team (2021); R: A language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria; URL https://www.R-project.org/). Maps were generated by QGIS.org (2024; QGIS Geographic Information System; Open Source Geospatial Foundation Project; http://qgis.org).

Ethics Statement

The procedures adopted followed the Declaration of Helsinki. The study and all research procedures adopted were approved by the Research Ethics Committee of the Faculty of Medicine of the University of Brasília (47377121.7.1001.5558). Access to anonymised public data from the Federal Comptroller General's portal, known as Fala Brasil, was also authorised under the Brazilian Federal 12,527 Access to Information Law (available at: https://www.planalto.gov.br/ccivil_03/_ato2011-2014/2011/lei/l12527.htm). Every patient signed an informed consent form to have their data included on this secondary, anonymised data platform. Furthermore, Brazilian Federal Law No. 14,874/2024 (available at https://www.planalto.gov.br/ccivil_03/_ato2023-2026/2024/lei/l14874.htm) stipulates that additional consent is not required for research using public, secondary, anonymised databases.

Results

An examination of Brazilian social security records revealed that 32,512 benefits were granted for psoriasis from 1998 to 2023. This amounted to an expenditure of $577,478,002.15 over the 25-year period studied. The mean age of patients receiving benefits from sick leave for psoriasis patients was 45.43 years (SD = 10.73). In total, 13,728 were female, and 18,784 were male. Among the total sample, 4187 benefits were still active at the time of the evaluation. Patients diagnosed with generalised pustular psoriasis (GPP) (L40.1) had a shorter mean duration of sick leave benefits (120.07 weeks) than did patients diagnosed with psoriasis (L40) (164.22 weeks) (p = 0.001)(Supplementary Table 1).

Evolution of the Annual Average Minimum Wage Received by Patients with Psoriasis with Sick Leave from 1998 to 2023

With respect to the average number of minimum wages received monthly, a pattern of increase was identified, starting from 2.34 in 1998 and peaking at 2.52 in 2000. A decline in the average minimum wages received at the beginning was subsequently observed, reaching a value of 1.22 in 2023. Brazil has a total of 5570 municipalities. Of the periods analysed, there was an increase in the number of Brazilian municipalities with beneficiaries until 2013, when 868 municipalities had at least one person receiving aid. Beginning in 2014, when target medications were included for PsA in the public system, this number decreased to 435 municipalities with beneficiaries in 2023 (Figure 1).

The adjusted GLM analysis (Figure 2) revealed that being male (compared with being female) increased the average minimum wage by 37% (AR = 1.37; 95% CI: 1.35–1.38). Compared with living in the Brazilian North region, residing in the Southeast region increased the average minimum wage by 18% (AR = 1.18; 95% CI: 1.14–1.22). On the other hand, residing in the Northeast region reduced the average minimum wage by 14% (AR = 0.86; 95% CI: 0.83–0.89), and no significant difference was found for individuals in residing in the Central-West region (AR = 1.02; 95% CI: 0.98–1.07). Notably, public access to PsA-targeted therapies decreased the average minimum wage granted by 22% (AR = 0.78; 95% CI: 0.77–0.80), and public access to psoriasis-targeted therapies reduced the average wage by 7% (AR = 0.93; 95% CI: 0.91–0.96). This analysis did not identify any influence of age on the granting of benefits (AR = 1.00; 95% CI: 0.99–1.00).

Impact of the Incorporation of Targeted Therapies for PsA

To analyse the impact of integrating targeted therapies for PsA into the Brazilian Unified Health System, we evaluated the provision of 10,869 benefits to psoriasis patients from 1998 to 2023. Psoriasis patients who received social benefits during the period when targeted therapies were available for PsA exhibited a notably faster return to work, as demonstrated by the survival curve (Figure 3). Furthermore, a positive association was observed between the availability of targeted therapies for PsA and reduced sick leave duration in the adjusted proportional hazards model (HR = 1.90; 95% CI = 1.82–2.00; p < 0.001) (Figure 3)(Supplementary Data 1).

Impact of the Incorporation of Targeted Therapies for Psoriasis

To analyse the impact of integrating targeted therapies for psoriasis into the Brazilian healthcare system, we evaluated the provision of 10,722 benefits to psoriasis patients from 1998 to 2023. Psoriasis patients who received social benefits during the

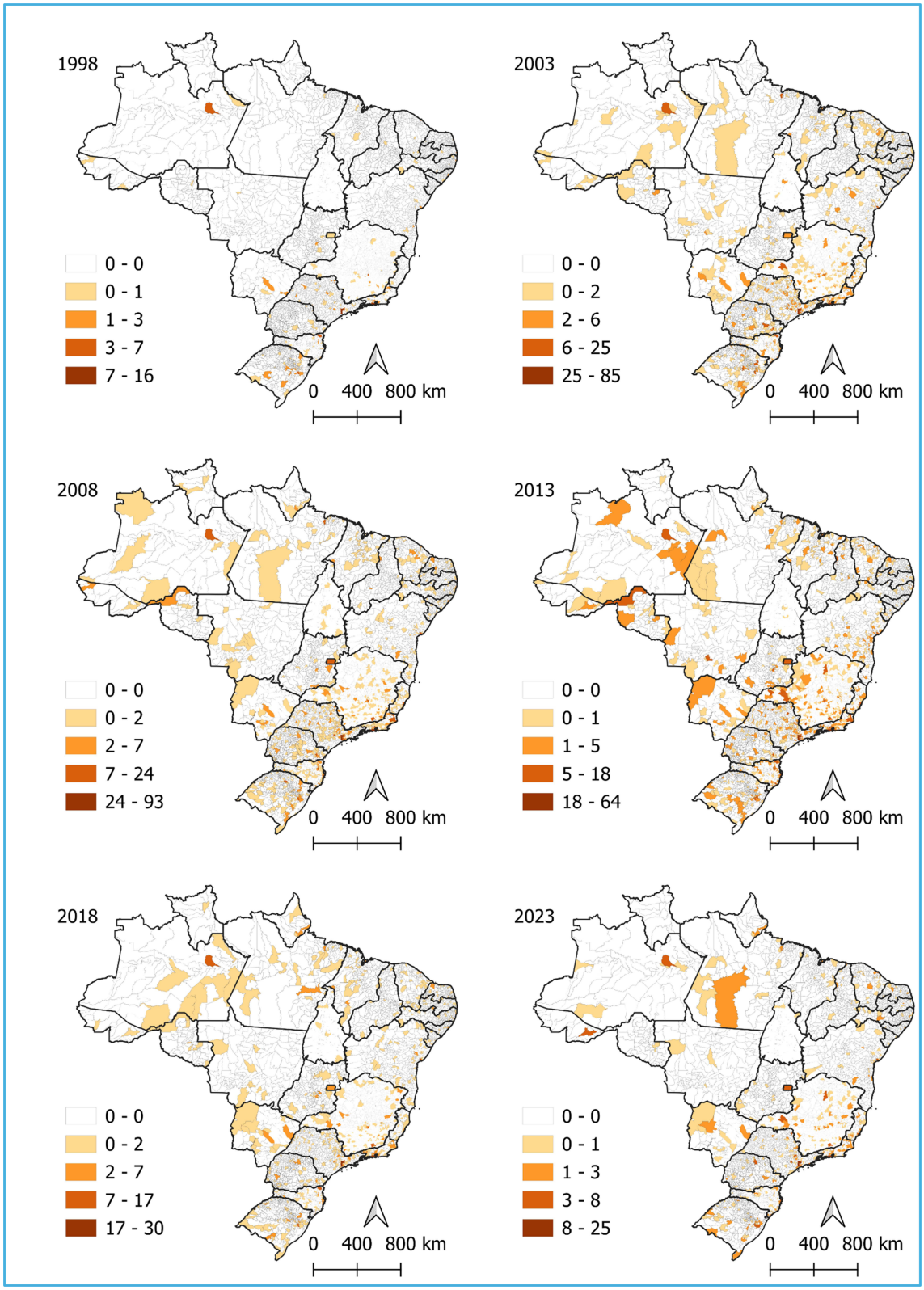

Figure 1 Consecutive maps showing that there was an increase in the number of Brazilian municipalities with beneficiaries until 2013, where 868 municipalities had at least one person receiving aid. From 2013 onwards, this number decreased, with 435 municipalities with beneficiaries in 2023. Maps generated by QGIS.org (2024). QGIS Geographic Information System. Open Source Geospatial Foundation Project. http://qgis.org.

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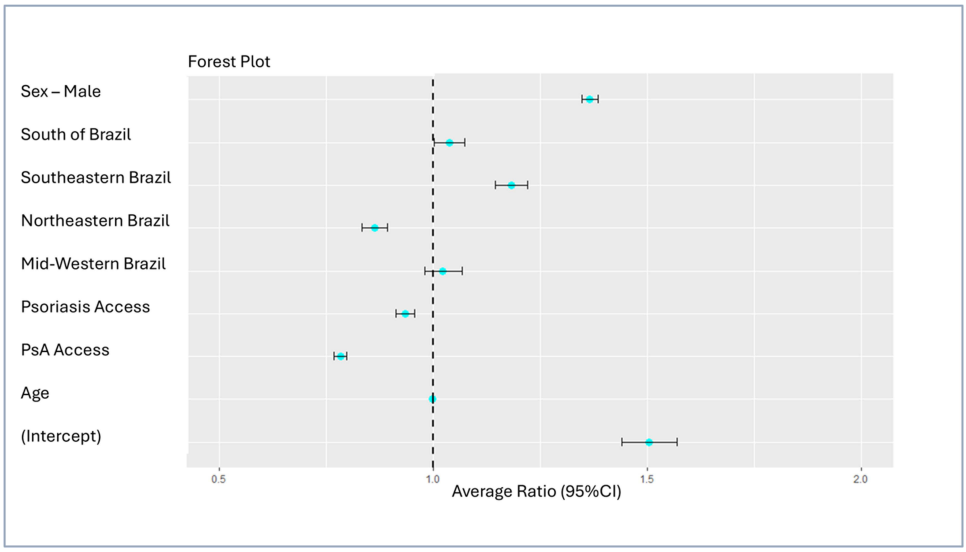

Figure 2 A forest plot showing the results of the generalised linear model (GLM) with the log link function and gamma family. The results were exponentiated and represented as average ratios (95% confidence intervals). Public access to PsA-targeted therapies decreased the average minimum wage granted by 22% (average ratio (AR) = 0.78; 95% CI: 0.77–0·80), and public access to psoriasis-targeted therapies reduced the average wage by 7% (AR = 0.93; 95% CI: 0.91–0.96). Legend: PsA = psoriatic arthritis.

period when targeted therapies were available for psoriasis exhibited a notably faster return to work, as demonstrated by the survival curve (Figure 4). Furthermore, a positive association was observed between the availability of targeted therapies for psoriasis and reduced sick leave duration in the adjusted proportional hazards model (HR = 1.63 95% CI = 1.54–1.70; $p < 0.001$) (Figure 4). In this model, male psoriasis patients were slower at returning to work from sick leave than female patients were (HR = 0.96; 95% CI = 0.99–1.00; p = 0.027) (Figure 4). Additionally, older patients reported a slower return to work from sick leave (HR = 0.99; 95% CI = 0.99–1.00; $p < 0.001$) (Figure 4)(Supplementary Data 2).

Comparison of the Impact of the Incorporation of Targeted Therapies for Psoriasis with That of the Incorporation of Targeted Therapies for PsA

To further analyse the impact of integrating effective targeted therapies for psoriasis into the Brazilian Unified Health System, particularly when biologics for PsA are already available, we evaluated the provision of 2820 benefits to psoriasis patients from 2015 to 2023. No additional reduction in sick leave duration was observed with the incorporation of targeted therapies for psoriasis in comparison with the earlier incorporation of effective targeted therapies for PsA. In fact, a slightly shorter sick leave duration was noted for patients with access to PsA-targeted effective therapies (HR = 0.90; 95% CI = 0.84–0.97; p = 0.006). Age and male sex were again associated with longer sick leave durations (Figure 5)(Supplementary Data 3).

Discussion

Countries in the Global South have undergone significant demographic and economic development, raising concerns about their future ability to finance high-cost health advancements and sustain health expenditures.[11,12] To partially address this significant challenge, governments must adopt high standards for cost-effectiveness analyses, accounting for both the direct and indirect impacts of new technologies.[13] Although most countries rely on the evaluation of direct costs, there is an urgent global need to develop feasible methods that include indirect costs in decisions regarding technology acquisition for large populations, given that healthcare-related costs are far more complex than the direct costs of medical supplies.[10,14–19]

In the present study, data gleaned from over 30,000 benefits granted to psoriasis patients revealed an intriguing trend. Following a notable surge in expenditure from 1998 to 2000, a gradual decline in the annual average minimum wage spent by the system on these patients emerged. The early 2000s were a transformative era in Brazil and globally, marked

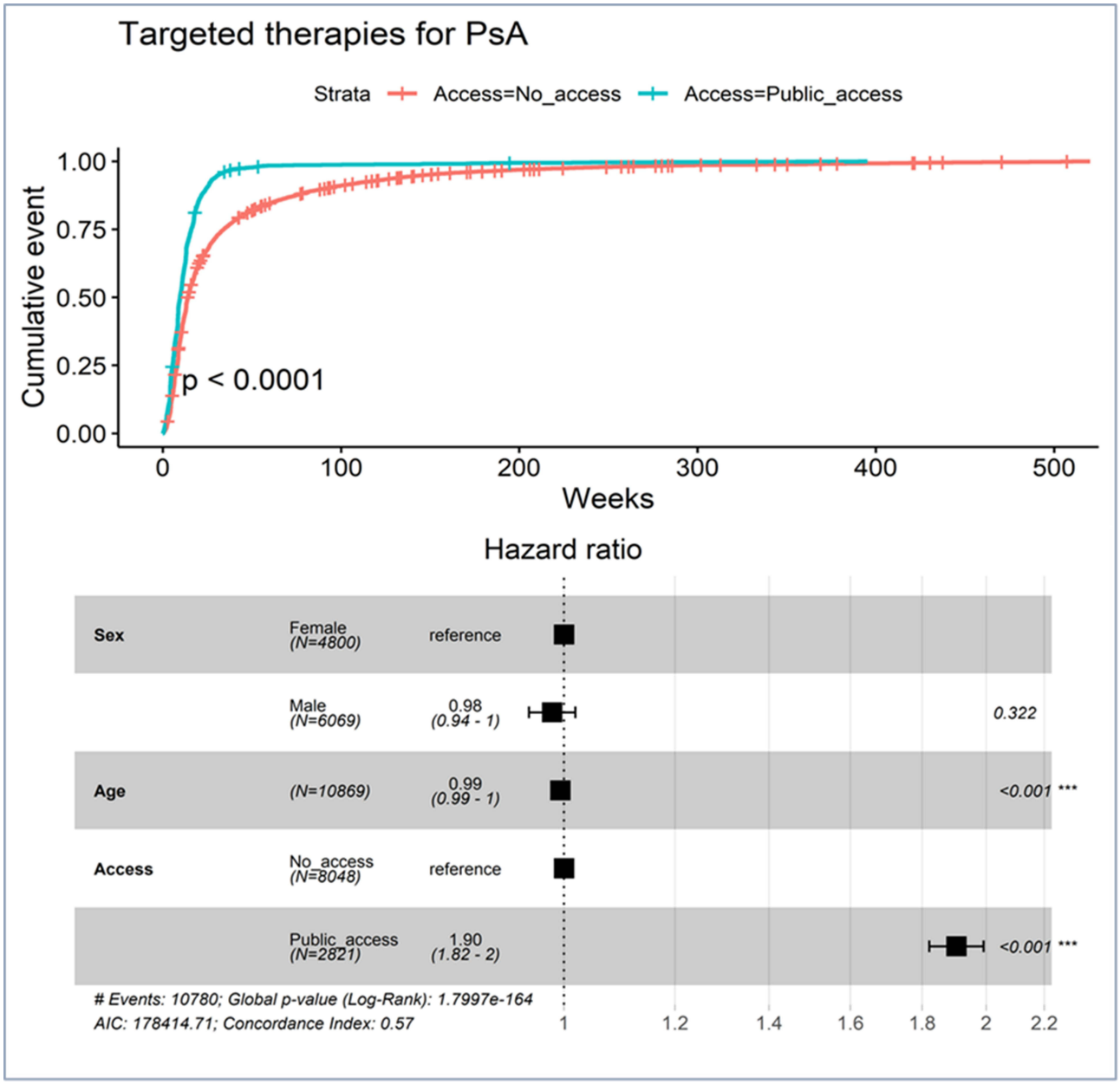

Figure 3 The survival curve shows that psoriasis patients who received social benefits during the period when targeted therapies were available for PsA exhibited a notably faster return to work. A positive association was observed between the availability of targeted therapies for PsA and reduced sick leave duration in the proportional hazards model. Legend: PsA = psoriatic arthritis. ***P < 0.001(Supplementary Data 1).

by the swift ascent of targeted therapies for various immune-mediated conditions. Among these, biological TNF alpha (α) blockers stand out for their diverse applications in rheumatology, extending to psoriasis treatment. In Brazil, the introduction of the first anti-TNF agent, infliximab, into the Brazilian Unified Health System for rheumatoid arthritis in 2002 paved the way for subsequent additions, such as etanercept in 2006 and adalimumab in 2010.[20] Although these incorporations were initially specific to rheumatoid arthritis, they indirectly benefited many psoriasis patients because of the lack of stringent control over their dispensation. Furthermore, during this period, these biologics became increasingly accessible for psoriasis treatment through supplementary health insurance systems and state-level incorporations. This availability of targeted therapies likely contributed to the reduction in psoriasis-related pension costs, an assertion bolstered by further analysis of specific incorporations for PsA and psoriasis discussed later in this study.

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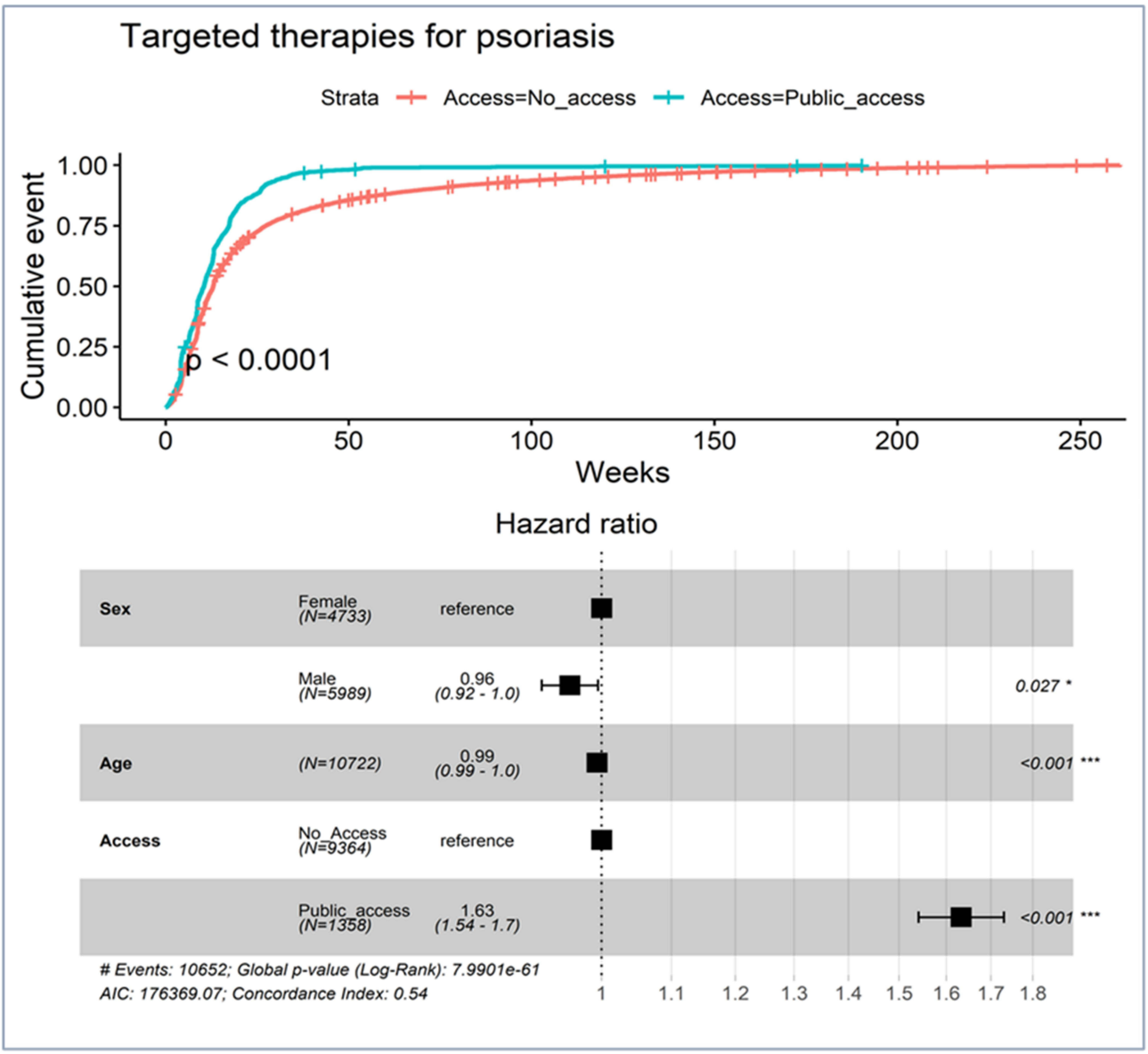

Figure 4 The survival curve revealed that psoriasis patients who received social benefits during the period when effective targeted therapies were available for psoriasis exhibited a notably faster return to work. A positive association was observed between the availability of targeted therapies for psoriasis and reduced sick leave duration in the proportional hazards model. *P < 0.05; ***P < 0.001 (Supplementary Data 2).

A total of $577,478,002.15 was spent on sick leave for patients directly impacted by psoriasis over the 25-year period studied. Although this figure is substantial, particularly for a developing country, it is undoubtedly an underestimate. Initially, one might not expect psoriasis—a disease that is completely manageable with the use of novel, effective targeted therapies—to directly result in the allocation of long sick leave benefits. However, the impact of psoriasis on the global social security system is likely much more closely related to its comorbidities, such as sequelae from PsA, depression, or associated cardiovascular events.

Previous studies have unequivocally demonstrated that the severity of psoriasis is a pivotal predictor of diminished work productivity.[21,22] Unfortunately, such specific information was not recorded within the Brazilian National Institute of Social Security system. Notably, this study revealed that male sex and older age were significantly associated with prolonged sick leave durations among psoriasis patients. Some earlier reports suggest that men may suffer from more severe manifestations of psoriasis.[23,24] Additionally, although elderly patients generally tend to have milder forms of psoriasis, they might be more susceptible to the broader, more debilitating impacts of psoriasis and its comorbidities in

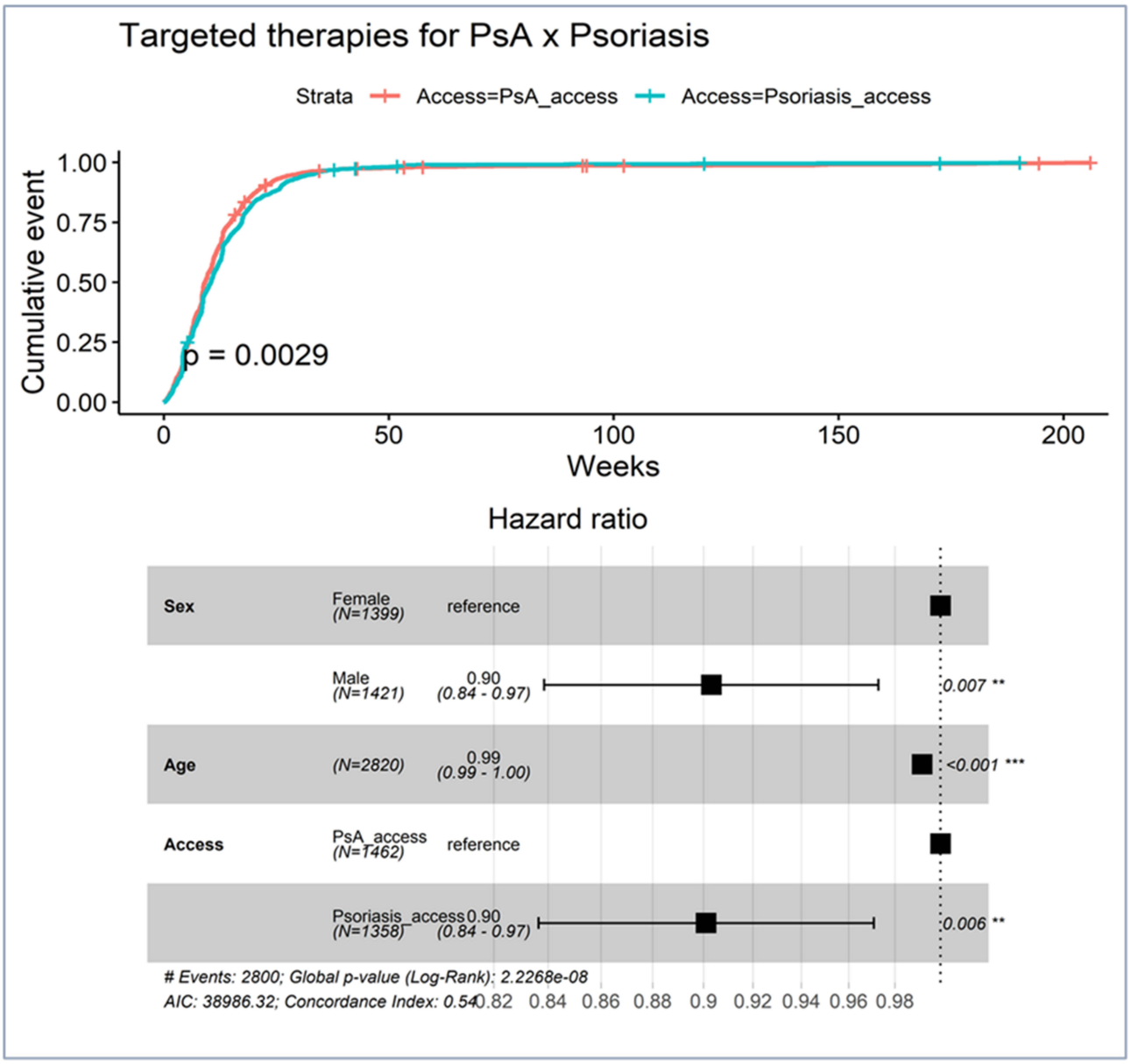

Figure 5 The survival curve revealed a slightly shorter sick leave duration for psoriasis patients with access to PsA-targeted therapies than for patients with access to psoriasis-targeted effective therapies. Age and male sex were associated with longer sick leave durations. Legend: PsA = psoriatic arthritis. **P < 0.01; ***P < 0.001 (Supplementary Data 3).

terms of their capacity to work. Patients with GPP presented a shorter average duration of sick leave benefits than did those diagnosed with psoriasis (L40). This outcome was anticipated given that GPP is recognised as an acute disease. GPP is a potentially life-threatening phenotype that may also influence the duration of sick leave.[25]

Our survival analysis revealed a significant reduction in the duration of psoriasis-related sick leave and associated costs following the introduction of public access to effective targeted therapies for PsA (Figure 3). In Brazil, the first implementation of targeted therapies for PsA occurred in 2014 with the introduction of TNF-α blockers. The impact of this implementation on data related to psoriasis can be explained by the close association between PsA and psoriasis. Most on-label medications indicated for PsA are also indicated for psoriasis, and up to one-third of psoriasis patients will develop PsA during the course of the disease.[26] Similarly, our survival analysis revealed a significant reduction in psoriasis-related sick leave duration and associated costs after the introduction of public access to targeted therapies for psoriasis, which was first offered in 2018 (Figure 4).

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Previous data support the idea that the introduction of effective large-scale therapies can improve quality of life and reduce indirect costs related to chronic diseases. In Brazil, a similar effect was observed after the inclusion of adalimumab for the treatment of hidradenitis suppurativa in the Brazilian Unified Health System.[10] Although there are limited data on large governmental systems, post hoc analyses of high-quality clinical trials, such as the CLEAR and FIXTURE studies, support this association.[27–29] In these trials, secukinumab not only proved to be more efficacious but also significantly reduced work impairment and the associated indirect costs of psoriasis compared with ustekinumab and etanercept from weeks 16 through 52 in the United Kingdom.[15] Similarly, the PSO-LONG trial revealed that the use of calcipotriol and betamethasone dipropionate foam for the long-term management of psoriasis not only improved skin health but also led to significant reductions in work productivity loss and activity impairment. These benefits translated into noteworthy indirect cost savings, painting a promising picture for the economic impact of effective psoriasis treatments.[30]

After the initial incorporation of PsA-targeted therapies in 2014 and specific psoriasis-targeted effective therapies in 2018, many additional therapies were incorporated into the Brazilian Unified Health System. Today, a wide range of options, such as IL-17, IL-12/23, IL-23, and Janus kinase (JAK) inhibitors, are available for the treatment of psoriasis and PsA. Our analytical model revealed a slightly shorter sick leave duration for psoriasis patients with access to PsA-targeted effective therapies than for patients with access to psoriasis-targeted therapies. Notably, rheumatological treatment for PsA is usually more intense than psoriasis treatment and is usually performed by combining biologics with classic immunosuppressants, possibly resulting in faster effects on the duration of sick leave. Additionally, because PsA usually results in more sequelae than psoriasis alone does, it is possible that many patients registered as having psoriasis at the Brazilian National Institute of Social Security also present with PsA, explaining the stronger effect of PsA-targeted therapies on the duration of sick leave benefits. The evolution of this effect must be continuously monitored because new and more effective drugs are being constantly developed for many types of immune-mediated diseases, leading to longer drug survival and effective psoriasis control, especially IL-23 and IL-17A/IL17F blockers.[31–33]

Although conducting complementary larger prospective cohort studies based on primary data is likely unfeasible, the main limitation of the present study is its reliance on secondary data. Despite these limitations, the study of the Brazilian National Institute of Social Security enables us to gather data from more than 30,000 patients over the past 25 years who were followed up for an extended period by occupational medicine specialists. Moreover, the present model has been previously validated and indicates a significant trend towards cost reductions and a decreased duration of sick leave following the specific incorporation of effective targeted therapies. Certain additional types of bias must always be considered in studies based on secondary data. Because PsA is a more disabling condition than is isolated psoriasis, the impact of PsA-targeted interventions might be more sensitively measured owing to a possible underreporting of psoriasis-related events. This is a common limitation when studying skin conditions given that nonspecialists may tend to underestimate the impact of the severity of skin conditions.

Conclusions

The findings of this study indicate a significant reduction in costs and sick leave durations following the implementation of therapies for psoriatic disease at the Brazilian National Institute of Social Security. It is crucial to consider detailed indirect cost data when including or reviewing new health technologies for large populations.

Abbreviation

PsA, Psoriatic arthritis.

Data Sharing Statement

Data from this study can be made available upon request.

Ethics Approval and Informed Consent

The procedures adopted followed the Declaration of Helsinki. The study and all research procedures adopted were approved by the Research Ethics Committee of the Faculty of Medicine of the University of Brasília

(47377121.7.1001.5558). Access to anonymised public data from the Federal Comptroller General's portal, known as Fala Brasil, was also authorised under the Brazilian Federal 12,527 Access to Information Law (available at: https://www.planalto.gov.br/ccivil_03/_ato2011-2014/2011/lei/l12527.htm). Every patient signed an informed consent form to have their data included on this secondary, anonymised data platform. Furthermore, Brazilian Federal Law No. 14,874/2024 (available at https://www.planalto.gov.br/ccivil_03/_ato2023-2026/2024/lei/l14874.htm) stipulates that additional consent is not required for research using public, secondary, anonymised databases.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

Prof. Ciro Martins Gomes is a consultant, lecturer and/or researcher for Boehringer-Ingelheim, Janssen, Novartis and AbbVie. Prof Gleison Duarte is a consultant, lecturer and/or researcher for Boehringer-Ingelheim, Pfizer, Leo Pharma, Amgen, UCB, Sanofi Genzyme, Janssen, Novartis and AbbVie. Luiza Ferreira Vieira d'Almeida is a lecturer for Novartis and AbbVie. The authors report no other conflicts of interest in this work.

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