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ORIGINAL ARTICLE

External validation of the Dat'AIDS score: A risk score for predicting 5-year overall mortality in people living with HIV aged 60 years or older

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Abstract

Objective: To perform an external validation of the Dat'AIDS score for predicting 5-year overall mortality among people with HIV (PWH) aged 60 years or older.

The Members of the Swiss HIV Cohort Study and contributing members of the Dat'AIDS Study Group members are given in Appendix A.

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Methods: This was a multi-centre prospective cohort study at all sites participating in the Swiss HIV Cohort Study (SHCS). We calculated the Dat'AIDS score in PWH aged 60 years or older at their first visit between 1 January 2015 and 1 January 2020. People living with HIV-2 and those whose Dat'AIDS score could not be calculated were excluded. Patients were followed until 1 January 2020. The primary endpoint was all-cause mortality. Vital status was collected throughout the study period. We obtained population and score descriptive statistics and assessed the score's discrimination and calibration.

Results: We included 2205 participants (82% male) of median [interquartile range (IQR)] age 62.0 (60.3–67.0) years, mostly with viraemia <50 copies/mL (92.7%). Median follow-up time was 15.9 years and median (IQR) CD4 cell count at enrolment was 586 (420–782) cells/μL. In all, 152 deaths were recorded during a total follow-up period of 7147 patient-years. The median (IQR) observed Dat'AIDS score was 3 (0–8). Discriminative capacities were good as the C-statistic was 0.73 (95% CI: 0.69–0.77) and consistent across all subgroups. Comparison of observed and expected survival probabilities showed good calibration.

Conclusions: External validation of the Dat'AIDS score in patients aged 60 years or older showed that it could be a useful tool not only for research purposes, but also to identify older patients at a higher mortality risk and to tailor the most appropriate interventions.

KEYWORDS
cohort studies, comorbidity, HIV infections/mortality, risk score, validation study

INTRODUCTION

Since the advent of combination antiretroviral therapy (cART), AIDS- and non-AIDS-related mortality have decreased and HIV infection has become a long-term chronic disease [1, 2]. Therefore, there is a new and growing older population with comorbidities among people with HIV (PWH) [3]. For example, around 12% of PWH actively followed in the Swiss HIV Cohort Study (SHCS) in 2019 were aged 65 years or older. Elderly PWH have a different epidemiology in terms of many clinical outcomes, as compared with HIV-uninfected populations of the same age. The burden of comorbidities is high in this population [4, 5] and will likely continue to increase [3]. Comorbidities, especially chronic renal disease and cardiovascular diseases, as well as non-HIV-related malignancies, may play an important role in their life expectancy, at least as important as HIV-related factors such as CD4 cell count and HIV viral load [6, 7].

This different epidemiology characterised by a higher comorbidity burden indicates that a dedicated score specifically designed to estimate the mortality risk among older PWH has the potential to be useful in research and clinical practice [8]. For this purpose, the Dat'AIDS score has been derived and internally validated in the context of the Dat'AIDS cohort [9]. The Dat'AIDS score comprises simple, easily accessible and reliable predictors: that is, HIV-related factors such as CD4 cell count, and non HIV-associated factors such as age and comorbidities (Table S1). Of note, candidate variables for the score such as HV-1 viral load >50 copies/mL, AIDS diagnosis or CD4 nadir were not found to be significant predictors to include in the Dat'AIDS score, highlighting the predominant burden of comorbidities in this population. The Dat'AIDS score theoretically ranges from 0 to 73, although observed scores in the derivation study ranged from 0 to 45 [9]. The score allows four risk groups to be identified, ranging from low-risk to very high-risk, with the low-risk group and the very high-risk group having expected probabilities of 5-year mortality of 5% and 46%, respectively. The score has previously shown good discrimination (C-statistic, 0.76, 95% CI: 0.71–0.79) and good calibration. It was well evaluated only for scores ranging up to 30–35 (few patients are beyond these scores) and was derived in a European, high-income population. However, this score has not yet been externally validated [10].

Such a score can be useful to both researchers and clinicians. Preventive and therapeutic strategies could be refined according to risk groups and it could also improve risk assessment by clinicians. The score could be used as an adjustment variable for comorbidities in observational studies or as an inclusion criterion, especially for clinical trials whose primary endpoint includes death. In this context, an external validation of the score is mandatory before its widespread use. Therefore, the aim of this study was to externally validate the Dat'AIDS score's capacity to predict 5-year overall mortality in PWH aged 60 or older, using data from the SHCS.

MATERIALS AND METHODS

Study design and population

This was a multi-centre, prospective cohort study in all sites participating in the SHCS (www.shcs.ch), a systematic longitudinal study enrolling HIV-infected individuals in Switzerland since 1988 [11]. We included all HIV-1-infected individuals who had at least one cohort visit during the study period (1 January 2015 to 1 January 2020) at which they were aged 60 or older. The first of these visits was the individual's study baseline. We continued to follow them up to the last known follow-up date or date of death or 1 January 2020 (study exit date), whichever came first. We excluded PWH with HIV-2 and those whose Dat'AIDS score could not be calculated due to missing data.

The Dat'AIDS score

The Dat'AIDS score is a mortality prediction score for elderly PWH that has been developed and internally validated on 1415 patients (age ≥ 60 years) included in the Dat'AIDS cohort [9] (NCT 02898987 ClinicalTrials.gov), a prospective French multi-centre cohort of PWH established in 2000. As of 31 December 2018, it comprised 24 French public hospitals, including French overseas territories (the islands of Martinique and Guadeloupe in the Caribbean). It covers approximately one-half of the PWH in care in France, with more than 80 000 patients currently included. The Dat'AIDS score comprises the following predictors: age, CD4 cell count, non-HIV related cancer, cardiovascular disease, estimated glomerular filtration rate (eGFR), cirrhosis, low body mass index (BMI) and anaemia. The associated points attributed to each predictor are summarized in Table S1. The Dat'AIDS score ranges from 0 to a maximal value of 73. During derivation, the range was divided into four risk groups: low-risk (0–3 points); moderate risk (4–13 points); high-risk (14–19 points); and very high-risk (≥ 20 points).

Primary endpoint

The primary endpoint was all-cause mortality. Vital status was collected throughout the study period. For patients lost to follow-up before the exit date, vital status was retrieved in medical files, when available. If the vital status could not be updated, the patients were censored at the latest date known alive after checking the medical file.

Data collection

We collected the following data at baseline: age; date of HIV diagnosis; sex at birth, height (m); weight (kg); ethnicity; main HIV acquisition risk group; current ART regimen; CD4 cell count and CD4 cell count nadir (cells/μL); HIV-1 RNA (copies/mL); AIDS status; time on ART treatment; ART received; creatinine serum level (μmol/L); haemoglobin (g/dL); history of non-HIV cancer; cardiovascular disease; and cirrhosis. For laboratory measurements, we considered only variables collected from 3 months before up to 1 month after the entry date, and selected the closest from the entry date.

The eGFR (mL/min/1.73 m^2) was calculated at baseline using the CKD-EPI formula [12] and the BMI was calculated at baseline as weight (kg)/height^2 (m^2). Low BMI and anaemia were defined as BMI < 18.5 kg/m^2 and haemoglobin <13 g/dL for males or haemoglobin <12 g/dL for females, respectively, as in the derivation study [9].

Non-HIV-related cancers, cirrhosis and cardiovascular disease were defined using the HIV Cohorts Data Exchange Protocol codes corresponding to the ICD-10 codes used in the derivation study [9]. However, unlike the Dat'AIDS cohort, the SHCS cohort lacked congestive heart failure (CHF) data. Using the derivation dataset, we evaluated the influence of CHF on the Dat'AIDS score by comparing its value with and without using CHF in the definition of cardiovascular disease. Only 33 of 1366 patients (2.4%) included in the original study had lower Dat'AIDS scores without taking CHF into account, while the score remained the same for the other patients. Moreover, after redeveloping the score without CHF, we found that Harrell's C-statistic remained very similar with and without this variable. Thus, we judged it was reasonable to assess the external validation of the Dat'AIDS score without CHF data.

TABLE 1 Characteristics of Swiss HIV Cohort Study (SHCS) patients included in the Dat'AIDS score validation study.

SHCS patient characteristics	$N = 2205$[1]
Sex at birth	
Female	408 (18.5%)
Male	1797 (81.5%)
Age (years)	62.0 (60.3, 67.0)
HIV acquisition risk group	
Homosexual contact	1023 (46.4%)
Heterosexual contact	885 (40.1%)
Intravenous drug use	192 (8.7%)
Other	31 (1.4%)
Unknown/inconclusive	74 (3.4%)
Viral load	
<50 copies/mL	2040 (92.7%)
≥50 copies/mL	160 (7.3%)
Unknown	5
CD4 (cells/μL)	586 (420–782)
Nadir CD4 (cells/μL)	160 (70–268)
Time from HIV diagnosis (years)	18 (10–25)
Unknown	260
Type of ART	
2 NRTIs +1 INI	627 (29.3%)
2 NRTI s+ 1 NNRTI	697 (32.6%)
2 NRTIs + 1 PI	294 (13.8%)
Dual therapy	40 (1.9%)
Other	467 (21.9%)
No therapy	12 (0.6%)
Unknown	68
Dat'AIDS variables	
Age (years)	
60–64	1463 (66.3%)
65–74	614 (27.8%)
≥75	128 (5.8%)
CD4 (cells/μL)	
<200	97 (4.4%)
200–350	290 (13.2%)
350–500	420 (19.0%)
≥500	1398 (63.4%)
Non-HIV-related cancer	70 (3.2%)
Cardiovascular disease	308 (14.0%)
eGFR[2]	
<30 mL/min/1.73 m^2	19 (0.9%)
30–59 mL/min/1.73 m^2	385 (17.5%)
≥60 mL/min/1.73 m^2	1801 (81.7%)
Cirrhosis	43 (2.0%)
Low BMI[3]	101 (4.6%)
Anemia[4]	240 (10.9%)

Abbreviations: ART, antiretroviral therapy; BMI, body mass index; eGFR, estimated glomerular filtration rate; INI, integrase inhibitors; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; PI, protease inhibitor.

[1] *n* (%) for qualitative variables; median (IQR) for quantitative variables.

[2] eGFR is defined according to the CKD-EPI formula.

[3] Low BMI is defined as BMI <18.5 kg/m^2.

[4] Anaemia is defined as a haemoglobin level <12 g/dL for females and <13 g/dL for males.

Statistical analysis

We used median and IQR and total numbers (percentages) to describe population characteristics. As the Dat'AIDS score is aimed for prognostic purposes, it was only calculated at baseline and not in a time-dependent manner. We evaluated the discrimination capacity of the Dat'AIDS score using the C-statistic [13] and hazard ratios between risk groups in a Cox model. In addition, the C-statistic was evaluated in the following subgroups: gender; CD4 count (<350 or ≥350 cells/μL); CD4 nadir (<200 or ≥200 cells/μL); HIV-1 RNA load (<200 or ≥200 copies/mL); and age (<65 or ≥65 years). A C-statistic <0.6 was regarded as of no clinical value, 0.6–0.7 of some clinical value, 0.7–0.8 as good discrimination, and >0.8 as an indication of excellent discrimination [14–16].

Calibration of the Dat'AIDS score was evaluated using the calibration slope computed on the Poisson process representation of a Cox model [17, 18]. Finally, we evaluated the agreement between predicted and observed survival probabilities for each risk group visually. Predicted probabilities were calculated using the baseline survival function of the derivation study as published [9]. Similar to preliminary analyses, there were more patients and deaths than in the derivation dataset and it was expected to have enough power to perform the external derivation of the Dat'AIDS score. Analyses were performed using R (R Core Team, 2022; R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/) with the survival [19] and tidyverse [20] packages. The Dat'AIDS score was computed using the hivscore R package developed by one of the study authors (JF, https://github.com/jaromilfrossard/). Results have been reported according to the TRIPOD checklist for prediction model validation [21].

RESULTS

Demographic and clinical characteristics

Among 2282 PWH aged 60 years or older followed in the SHCS during the study period, 2205 (96.6%) individuals were included in the study. Seventy-seven patients were excluded for the following reasons: missing CD4 count (17 patients), weight (37 patients), creatinine (14 patients) and haemoglobin (5 patients), and multiple missing variables (4 patients). Median (IQR) age of included PWH was 62.0 (60.3–67.0) years (male, 1797; 81.5%), under cART for a median time of 15.9 years, and immunologically and virologically controlled with a median (IQR)

TABLE 2 Description of pre-specified risk groups of the Dat'AIDS score in the Dat'AIDS score validation study.

Risk groups	Score value	Median observed score*	Number of patients*	5-year prediction[a]	Observed number of deaths	5-year observed survival probability*,[b]
Low-risk	0–3	0	1191	0.96	35	0.96 (0.94–0.97)
Moderate-risk	4–13	8	776	0.90	61	0.89 (0.87–0.92)
High-risk	14–19	16	154	0.77	32	0.75 (0.67–0.83)
Very high-risk	≥20	23	84	0.55	24	0.65 (0.54–0.78)

*In the validation dataset.
[a]5-year predicted probability of survival use the baseline hazard published in the derivation article [9].
[b]Kaplan–Meier estimates and 95% confidence intervals.

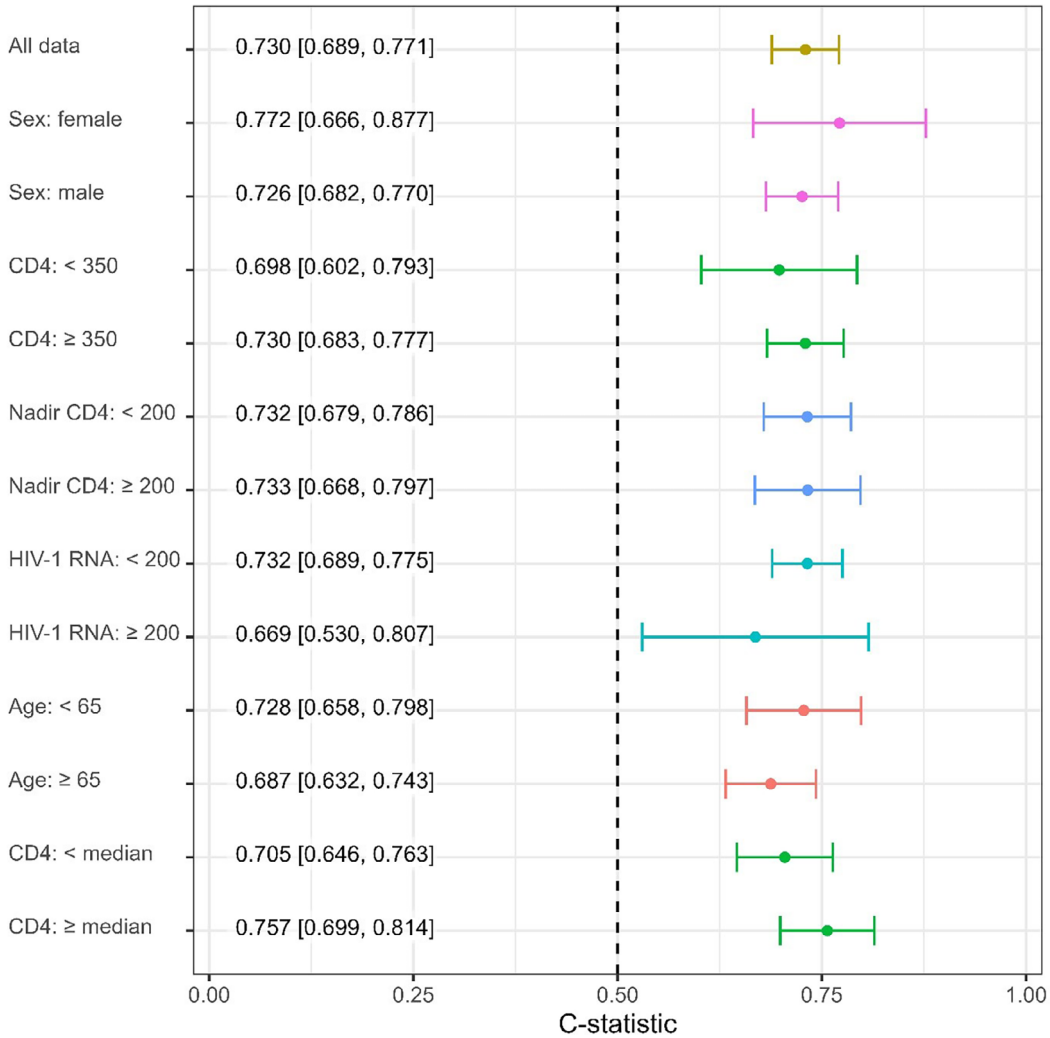

FIGURE 1 Harrell-C statistics of the Dat'AIDS score evaluated on the validation dataset and in subgroups.

TABLE 3 Model discrimination: hazard ratios across pre-specified risk groups of the Dat'AIDS score.

Risk groups	Hazard ratio	95% confidence interval	*P*-value
0–3 vs. 4–13	2.50	1.65–3.79	<0.001
4–13 vs. 14–19	2.65	1.73–4.07	<0.001
14–19 vs. ≥20	1.57	0.92–2.66	0.10

CD4 count of 586 (420–782) cells/μL; 2040 (92.7%) had a viral load <50 copies/mL. Baseline patient characteristics are shown in Table 1, as well as the distribution within each level of the predictors of the Dat'AIDS score. In our sample, 1191 (54.0%) PWH were in the low-risk group, 776 (35.2%) in the moderate-risk group, 154 (7%) in the high-risk group, and 84 (3.8%) in the very high- risk group. Vital status update was requested for 119 patients. We had

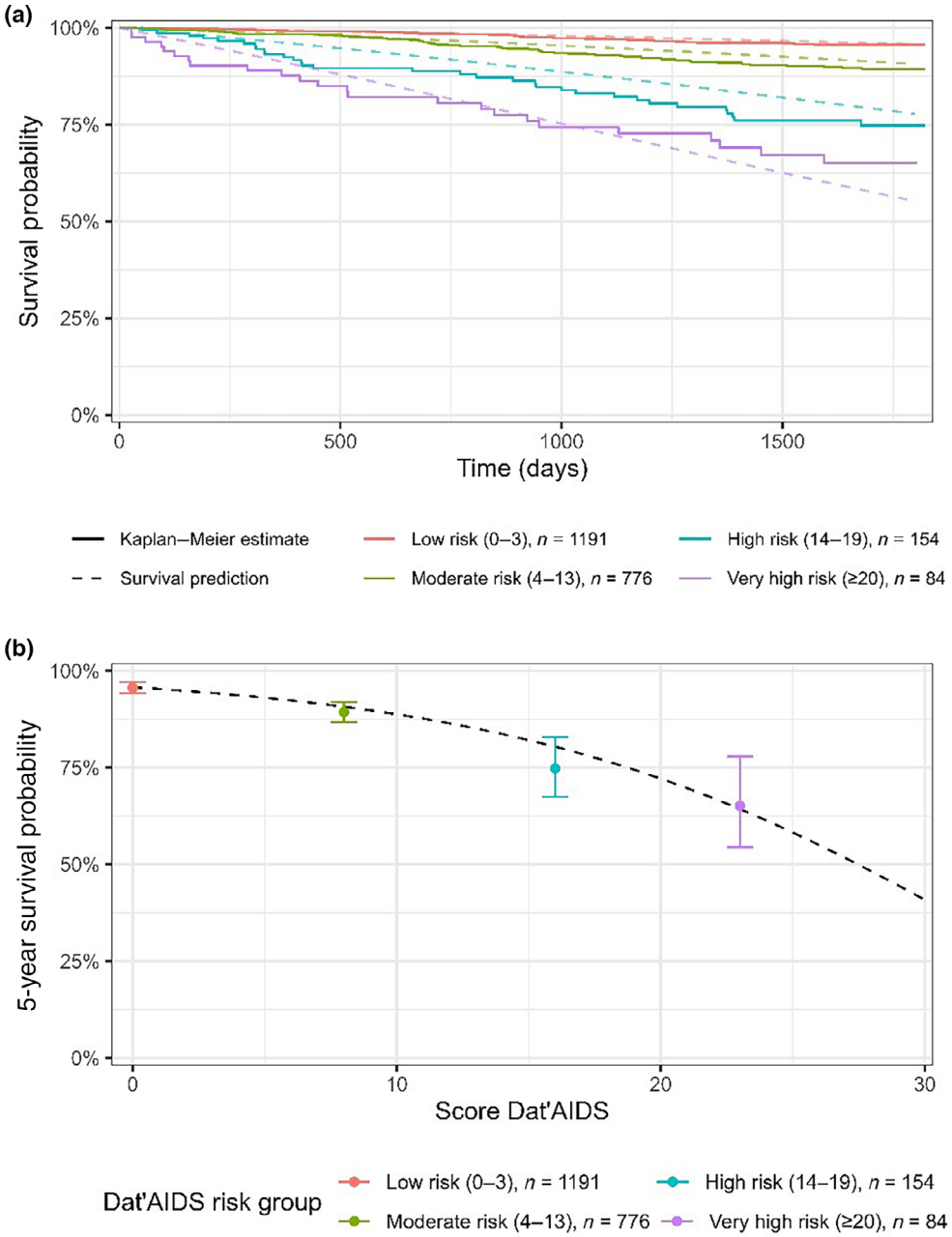

FIGURE 2 Calibration assessment of the Dat'AIDS score. (a) Observed survival (continuous, Kaplan–Meier curves) and predicted survival (dashed curves) probabilities by pre-specified risk group. For each risk group, the observed and predicted survival probabilities were similar, suggesting good calibration. Predicted probabilities were calculated using the baseline survival function of the derivation study as published [9]. (b) Five-year observed survival probability and 95% confidence intervals per risk group and predicted survival probability (dashed line) obtained by the Dat'AIDS score. Predicted probabilities have been calculated using the baseline survival function of the derivation study. Observed probabilities have been centred on the graph on the median score of each score group.

feedback from participating centres for 106 patients out of 119 (89%). Among those, date of last follow-up was updated for 15 patients (14%), and 9 deaths (8%) were retrieved during the study period. Finally, 152 deaths were recorded during a follow-up period of 7146.7 patient-years (PY) (2.12/100 PY). The median observed Dat'AIDS score was 3 (IQR 0–8). The distribution of pre-specified risk groups, as well as the corresponding 5-year observed mortality (using Kaplan–Meier estimate) and expected survival probabilities are presented in Table 2.

Discrimination assessment

The C-statistic was 0.73 (95% CI: 0.69–0.77) in the validation dataset and ranged between 0.67 and 0.77 across subgroups (Figure 1). The Dat'AIDS score divided into the pre-specified groups showed a good discrimination capacity as there was strong evidence of differential survival between the low- and moderate-risk groups and the moderate- and high-risk groups (Table 3). However, the difference between the high- and very high-risk groups was less pronounced, while the uncertainty was larger, owing to the smaller number of patients in these groups.

Calibration assessment

The Dat'AIDS score slightly overestimated the mortality rate of the very high-risk group (Table 2). As a result, its calibration slope was below 1 and estimated at 0.84 (95% CI: 0.68–0.99). Figure 2 shows the observed and predicted 5-year survival probabilities, as well as survival curves for each risk group. Observed and expected survival curves were close in the low-, moderate- and high-risk scores, which suggested a good calibration of the Dat'AIDS score in these groups. In the very high-risk group, the observed probability was higher than the predicted one (Figure 2a). However, this difference in calibration did not remain when displaying the observed survival compared with the expected survival at the level of the median observed score of each subgroup (Figure 2b), thus suggesting good calibration.

DISCUSSION

Developing prognostic indexes specific to older PWH is considered a research priority [8], due to the epidemiological pattern of the HIV epidemic worldwide [3]. In this study, we present the external validation of the French DAT'AIDS prognostic score performed in the context of the nationwide SHCS. We demonstrated that the score showed a good discrimination capacity and calibration, thus confirming its ability to accurately estimate survival probability over a 5-year period.

In more detail, the discrimination capacity of the Dat'AIDS score was found to be good (C-statistic 0.73, 95% CI: 0.69–0.77) and very similar to the one estimated in the derivation study, that is, 0.76. Specifically, we only observed a small decrease in C-statistic from the derivation to the validation study, which is expected as the score is likely to be better fitted in the population in which it was derived [22]. Moreover, it was consistent across all subgroups. Discrimination across the four pre-specified risk groups was good. More specifically, we found that the hazard ratios between the low-, moderate- and high-risk groups were comparable to those observed in the derivation study. Discrimination between the high- and very high-risk groups was less pronounced than in the derivation study [hazard ratio 1.57 (0.92–2.66) vs. 2.36 (1.48–3.78) in the derivation study]. This can probably be explained by the fact that the very high-risk group comprised less severely ill patients in the validation study compared with the derivation study, as the medians of the Dat'AIDS score in the very high-risk groups were 23 and 25, respectively. Moreover, there were fewer patients in the very high-risk group in the validation study compared with the derivation study (84 vs. 114), thus leading to reduced statistical power.

Regarding calibration, an overestimation of mortality towards the high end of predicted risks was observed with the Dat'AIDS score. This is probably due to a difference in the baseline risk of death between the French derivation cohort and the Swiss validation cohort. Indeed, the validation cohort comprised proportionally fewer patients in the high- and very high-risk groups. Moreover, patients were included in the period 2015–2020 in the validation cohort, compared with 2008–2013 in the derivation cohort, which implied a higher median CD4 count and higher rate of patients with virological control in the validation cohort [586 vs. 507 cells/μL (93% vs. 77%), respectively]. By contrast, the validation cohort had a longer duration of known HIV infection and ART exposure [9]. Nevertheless, we observed a very good concordance between the 5-year observed and expected survival probability in the low-, moderate- and high-risk groups. The 10% difference between observed and predicted survival rates in the very high-risk group can probably be explained by the difference in the median Dat'AIDS score between the derivation and validation studies, as suggested by Figure 2b.

The Dat'AIDS score may be used in PWH aged 60 years or older to serve various aims. It could be useful to clinicians in performing a risk–benefit assessment in the context of clinical decision-making, with the objective of tailoring preventive interventions. It could also be

useful to researchers in adjusting or stratifying analyses. Finally, it could be useful as an inclusion criterion to select patients with a high risk of death, that is, the high- and very high-risk groups, which were associated with 5-year risk of death of 25% and 35%, respectively.

At present, two prognostic indices have been used in these patients: the Veterans Aging Cohort Study (VACS) index 1.0 [23] and 2.0 [24]. The VACS index 1.0 includes age, CD4 count, HIV-1 RNA, haemoglobin, platelets, aspartate and alanine transaminase, creatinine, and viral hepatitis C infection. It has recently been updated and the version 2.0 adds BMI, white blood cell count and albumin level [24]. They have been validated in a largely European sample which included Swiss and French data (ART-CC) [25, 26]. However, despite showing a better discrimination capacity than the 1.0 version, the VACS index 2.0 may be harder to use, particularly when using data from existing observational studies, due to variables not routinely collected in clinical practice, especially the albumin level [24], although it might be possible to impute it, assuming that albumin is normal if missing as that would be the clinical assumption in most cases. Moreover, the VACS indices have not been specifically designed for the ageing PWH population. In patients aged 50 years or older (mostly 50–60 years old, although about one-quarter of the development cohort of the VACS index 2.0 was 60 years or older, which was not the case in the validation cohort [24]), the VACS indices 1.0 and 2.0 had similar C-statistics of 0.75 and 0.77, respectively, in the VACS and NA-ACCORD cohorts [22]. To date, it is still unclear how these other existing scores compare with the Dat'AIDS score as no data are available on their specific performance in PWH aged 60 years or older, which is expected to be predominant in future years. This age cut-off of 60 years seems particularly adapted to western countries where the standard geriatric age cut-off is 65 years with comorbidities, while taking into account the fact that PWH currently have a comorbidity profile and a biological age of matched HIV-uninfected people that are 5–10 years older than they are [5, 27]. Therefore, in order to help clinicians and researchers choose the more appropriate index in a specific context, comparison studies in cohorts independent of derivation cohorts are needed.

The Dat'AIDS score has unique strengths for a prognostic score. It is easy to calculate and can be used in everyday clinical practice, as well as for research purposes, for example using large existing databases, as it contains simple and reliably measured predictors such as age, CD4 count, history of non-HIV-related cancer, history of cardiovascular disease, eGFR, cirrhosis, BMI and anaemia, which are all easily obtainable at assessment [9].

Our study has some limitations. First, in contrast to the original Dat'AIDS score, CHF was not included in the definition of cardiovascular diseases as it was not recorded in the context of the SHCS. However, as shown by our analyses, the prevalence of this comorbidity is low and its absence is unlikely to alter the performance of the Dat'AIDS score in a significant manner. Second, despite the fact that vital status was systematically checked in all patients lost to follow-up, it has not been retrieved from a national registry as this is not available in Switzerland. Nevertheless, the observed mortality (2.12/100 PY) was similar to another study using a national registry for vital status update and including PWH aged 60 or more (2.47/100 PY) [7]. Moreover, the mortality rates in Swiss male patients aged 60–64 and 65–69 in 2015 were 0.9/100 PY and 1.2/100 PY, respectively, which is much lower than observed in our study, making it unlikely to have a significant loss of deaths (https://apps.who.int/gho/data/view.searo.LT62230?lang=en). Third, causes of deaths could have been informative. Nevertheless, the purpose of the Dat'AIDS score is to predict all-cause mortality. Once validated, its ability in predicting specific causes of deaths should be assessed in separate studies. Fourth, despite the possibility that the difference between observed and expected survival in the very high-risk group might be explained by a less comorbid very high-risk group in the validation study than in the derivation study, a miscalibration of this group cannot be ruled out. Fifth, this study was performed in a western European, high-income context and these results may not be extrapolated to other populations with different ethnicities without further studies. Sixth, because of a low number of patients in some subgroups (such as detectable HIV viral load or CD4 count <350 cells/μL) we did not have sufficient study power to confirm its discrimination and calibration capacities in these subgroups. However, they represent a minority of those patients (17.6% had a CD4 count <350 cells/μL and 7.3% had an HIV viral load >50 copies/mL). Finally, we chose to stop follow-up on 1 January 2020 to exclude the COVID-19 era. Although we acknowledge that this led to a loss of statistical power, this choice was made to avoid interactions with the disease itself, but also with the impact on the healthcare system that could have made our results more difficult to interpret. Specific studies are under way to address this issue, as the functionality of the Dat'AIDS score for predicting all-cause deaths in the COVID-19 era or of COVID-19 related deaths may be of great clinical interest.

The Dat'AIDS score should be validated in other populations, such as in other continents, in younger PWH or in different socioeconomic contexts. In addition,

its association with other medical conditions should be assessed, especially geriatric negative outcomes such as frailty, falls, denutrition, hospitalization or institutionalization. Such a score may reflect the extra burden of multi-morbidity and polypharmacy in the aged PWH population [28]. To further increase its use and implementation, as well as to help the researcher, a R package has been developed by one of the authors as mentioned earlier. Development of a web calculator is also under consideration. Nevertheless, it should be recalled that the absence of specific comorbidities in the Dat'AIDS score (e.g. obesity, tobacco use, etc.) does not mean that these comorbidities have no prognostic role in this population and that they should not be the target of specific interventions. Choices were made towards achieving an equilibrium between the inclusion of the more prognostic variables and the need for simplicity and variables that are easy to obtain in order to allow the widespread use of such a score.

In conclusion, this study demonstrates the external validity of the Dat'AIDS score in patients included in the SHCS aged 60 years or more in the late cART era. The score showed a good discrimination capacity as well as good calibration. It may be a useful tool for research, as well as for risk assessment by clinicians, especially as the population of aged PWH is becoming increasingly predominant.

AUTHOR CONTRIBUTIONS

MH and AC designed the study. JD, EH, DB, PS, EB, SR, and AC were the representatives of their respective study centers. JF performed data management. JF and MH performed the statistical analyses. MH, JF, and AC wrote the first manuscript draft. AC was responsible for the overall supervision of the study. All authors reviewed and approved the study protocol. All authors critically reviewed the manuscript and approved the final version.

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CONFLICTS OF INTEREST

None of the authors has declared a conflict of interest related to this study.

DATA AVAILABILITY STATEMENT

The individual level datasets generated or analysed during the current study do not fulfil the requirements for open data access:

1. The SHCS informed consent states that sharing data outside the SHCS network is only permitted for specific studies on HIV infection and its complications, and to researchers who have signed an agreement detailing the use of the data and biological samples; and
2. the data is too dense and comprehensive to preserve patient privacy in people living with HIV.

According to Swiss law, data cannot be shared if data subjects have not agreed or data are too sensitive to share. Investigators with a request for selected data should send a proposal to the respective SHCS address (www.shcs.ch/contact). The provision of data will be considered by the Scientific Board of the SHCS and the study team, is subject to Swiss legal and ethical regulations, and is outlined in a material and data transfer agreement.

ETHICS STATEMENT

The study was performed in accordance with the principles of the Declaration of Helsinki and current Swiss legislation relating to biomedical research. The SHCS was approved by the local ethics committees of the participating centers.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX A

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