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ORIGINAL RESEARCH

Reference intervals of work ability and productivity loss and their use in patients with inflammatory rheumatic and musculoskeletal diseases

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ABSTRACT

Objectives To establish reference intervals (RIs) for work ability, at-work productivity loss and overall productivity loss in the general working population and to compare work ability and at-work productivity loss of patients with inflammatory rheumatic and musculoskeletal disease (iRMD) with this population.

Methods Cross-sectional analysis among patients with iRMDs and population controls without iRMDs having paid work and participating in a Dutch cohort study. They reported on three work outcomes: work ability (0–10), at-work productivity loss and overall productivity loss (0%–100%). A generalised additive model for location, shape and scale parameters was used to establish age-specific RIs and percentile curves for controls. The proportion of patients and controls below each percentile curve was compared.

Results 413 controls were included; 73% female, with mean age 53 (SD 10) years, 60% had high education, mean work ability was 8.7 (1.6), at-work productivity loss 6.3% (7.2) and overall work productivity loss 11% (25.6). Percentile curves illustrated that work ability and at-work/overall work productivity loss were worse with increasing age. For instance, for work ability, the 95% RI for 22 to 29-year individuals was 5.9–10, while for individuals between 50 and 59 years, it was 4.9–9.1. Patients compared with controls had worse work outcomes, especially for at-work and overall productivity loss.

Conclusion Work ability and productivity are not perfect in the general population, based on the newly developed RIs for the three work outcomes. This calls for caution to not overestimate the iRMD impact on work outcomes. Nevertheless, iRMD patients have worse work ability and higher work productivity loss, compared with controls.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Work ability and work productivity in employed individuals are unknown.

WHAT THIS STUDY ADDS

⇒ Reference intervals (RIs) for the work outcomes work ability, at-work and overall productivity loss for the general population are now available.
⇒ In the general working population, work ability and work productivity are not optimal, and these outcomes worsen with increasing age.
⇒ Educational level may modify the effect of increasing age on work outcomes.
⇒ Compared with population controls, inflammatory rheumatic and musculoskeletal diseases (iRMDs) have substantial additional impact on presenteeism.
⇒ The gaps between patients and the general population are larger for work productivity compared with work ability.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ In analogy to the use of growth curves to monitor the growth of children, work outcomes in patients with iRMDs or other chronic diseases should be interpreted taking into account the age-specific RIs developed in this study from the general population.
⇒ The application of age-specific RIs will decrease the risk of overestimation of the effect of health-related problems on work outcomes.

INTRODUCTION

Inflammatory rheumatic and musculoskeletal diseases (iRMDs) are among the leading causes of restrictions in work participation (WP).[1] WP refers to active engagement in paid work, including absenteeism and presenteeism. Absenteeism indicates the time missed from work due to health reasons (ie, sick leave or work disability) and presenteeism refers to the reduction in work ability or productivity loss while at work, due to health problems.[2 3] Generally, patients may transition between presenteeism and absenteeism with health status and contextual factors (CFs) determining those transitions.[4] From an economic perspective, productivity

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loss due to absenteeism or presenteeism may have negative financial consequences for the workplace and society and it has been suggested that presenteeism may even account for a larger proportion of monetary losses than absenteeism.[5–8]

Several studies have revealed a WP gap between patients with iRMDs and the general population. The majority of these studies focused on work status (ie, being employed or work disabled) or absenteeism, that is, sick leave. Few studies compared presenteeism or overall work productivity (absenteeism *and* presenteeism) between working patients with RMDs and population controls.[9 10] Although a substantial impact of iRMDs on such outcomes has been described, presenteeism also occurs in persons from the general population that have no iRMD, but may suffer from another (chronic) disease. Notwithstanding, studies assessing presenteeism in the general population are scarce.[11 12] A European survey evaluating working conditions in the general population found that 40% of the respondents had worked while they were sick for at least 1 day in the last 12 months, especially women.[13] Data from a systematic literature review suggested that higher age and lower education were associated with more severe presenteeism, while sex was not. In that same study, physically demanding jobs, such as those requiring increased muscular effort, poor work postures and poor ergonomic conditions, were also associated with worse work ability.[12]

To appropriately interpret work ability (difficulty in doing a job) and productivity (work being done) of a person with an iRMD, it is important to also know and take into account the ability/productivity of an average person from the general population, which is likely not optimal. Otherwise, there is a risk of overestimation of work impairment and productivity loss in patients with iRMDs.

Reference intervals (RIs) are usually defined as the central 95% of test results' distribution obtained from a healthy reference population.[14 15] They are a common decision support tool used for interpretation of development patterns, like the growth percentile curves used in paediatrics to monitor the growth of children,[16] or numerical pathology reports, like laboratory tests.[14]

This study aimed to (1) establish RIs and percentile curves for three commonly used work outcomes, namely work ability, at-work productivity loss and overall productivity loss in the general working population (without iRMDs) and (2) compare the proportion of patients and controls below each percentile curve.

METHODS

Study population

A cross-sectional analysis was nested within an ongoing prospective Dutch cohort study on COVID-19, including patients with iRMD and general population controls, with no chronic physical health impairment, meaning that they did not have any iRMD either.[17–19] Briefly, patients aged 18 years and older with iRMD from the Amsterdam Rheumatology and Immunology Center (Amsterdam, Netherlands), were enrolled in the cohort study between April 2020 and March 2021. All participants were asked (but not obliged) to recruit their own healthy control participant of the same sex, comparable age (difference of <5 years) and without an iRMD. Data collection for the current study was conducted in March 2022, beyond the peaks of the pandemic, when a survey on work characteristics and work outcomes was distributed by email.

For the development of the RIs of the WP measures, only data from the general population controls at working age (≥18 and <67 years old) reporting paid work (full-time or part-time with ≥12 working hours/week) were used.

Data collection

Clinical data was collected at baseline (inclusion date) on age, sex, (co)-morbidities (other than iRMDs, dichotomised as presence of at least one opposed to no (co)-morbidity) and the education level (low: no education, primary school or lower secondary school; middle: upper secondary school or post-secondary non-tertiary school; and high: bachelor, master or doctoral education). In March 2022, a specific WP survey was conducted, collecting data on current employment type (ie, permanent contract or other), employment status (ie, full-time or part-time) and job demands (eg, physical demands). Only individuals at working age (<67 years old) were included in this analysis.

Work ability and work productivity

Two self-reported measurement instruments assessing work ability and productivity loss in working persons were included, addressing three target domains: one reflecting work ability and two reflecting work productivity.

Work Ability Index

Current work ability was addressed by the first item of the Work Ability Index (WAI) that asks persons to rate their work ability as compared with their 'lifetime best' on a numeric rating scale (NRS) (range 0–10) (10=best ability).[20]

Work Productivity and Activity Impairment Scale

Health-related at-work productivity loss was assessed by item 5 of the Work Productivity and Activity Impairment scale (WPAI-presenteeism) that asks patients to indicate the level of productivity loss while working, on an NRS (range 0–10) (10=worst productivity). It represents the proportion of time spent at work (on the scale of 0%–100% (best to worst)) that is lost due to health-related problems, and is calculated as follows: (WPAI item 5/10×100).[21]

Overall work productivity loss combines the absenteeism and presenteeism questions of the WPAI (ie, items 2–5) and is calculated as: (hours missed due to health)/([hours missed due to health]+[hours actually worked])×100+[1−([hours missed due to health]/([hours missed due to health]+[hours actually

Table 1 Participants characteristics and work outcomes of the working population of controls and iRMDs

	Controls (n=413)	iRMD patients (n=903)	P value
Age, years	51.5 (9.9)	51.2 (9.9)	0.560
Female gender, n (%)	307 (74)	568 (63)	<0.001
(Co)-morbidities (≥1), n (%)	27 (7)	138 (15)	
Education			0.770
Low, n (%)	30 (10)	65 (11)	
Middle, n (%)	88 (30)	202 (34)	
High, n (%)	178 (60)	326 (55)	
Permanent contract job, n (%)	110 (27)	212 (24)	0.240
Full-time job, n (%)	205 (50)	503 (56)	0.047
Physically demanding job, n (%)	61 (16)	122 (15)	0.600
Work ability (0–10)	8.7 (1.6)	8.1 (2.0)	<0.001
At-work productivity loss (0%–100%)	7.5 (19.0)	16.6 (24.8)	<0.001
Overall productivity loss (0%–100%)	14.3 (28)	24.9 (32.2)	<0.001
bDMARDs, n (%)	2 (0.4)	397 (44)	<0.001
csDMARDs, n (%)	2 (0.4)	497 (55)	<0.001
tsDMARDs, n (%)	0 (0)	12 (1.3)	0.041
Steroids, n (%)	2 (0.4)	86 (9.5)	<0.001
Other immunosupresives, n (%)	1 (0.2)	27 (3)	0.002
Disease duration, years	NA	13.2 (10.3)	

Results reflect mean (SD) unless stated otherwise.
Missing data for controls and iRMDs: work ability, n=27 (6%) and n=62 (7%); productivity loss, n=22 (5%) and n=23 (2.5%); overall at-work productivity loss, n=55 (12%) and n=101 (11%); education, n=118 (28%) and n=310 (34%); job with permanent contract, n=7 (2%) and n=9 (1%); physically demanding job, n=42 (10%) and n=73 (8%). Values in this table reported as observed. A total of 3.7% of all values were imputed for the GAMLSS analyses (not all variables shown). Outcomes were not imputed.
iRMD's diagnoses included: rheumatoid arthritis (50.3%), followed by axial spondyloarthritis (18.6%), psoriatic arthritis (16.5%), systemic lupus erythematosus (6%) and others (8.6%—less than 3% for each disease, including juvenile idiopathic arthritis, vasculitis, reactive arthritis, polymyalgia rheumatica, gout, Sjögren's syndrome, etc).
(Co)-morbidities included: cardiovascular diseases, diabetes, obesity and pulmonary disease.
bDMARDs, biologic disease-modifying antirheumatic drugs; csDMARDs, conventional synthetic DMARDs; iRMDs, inflammatory rheumatic and musculoskeletal diseases; tsDMARDs, targeted synthetic DMARDs.

worked]))]×[degree health affected productivity while working]/10×100]. The total score represents the time unproductive due to absenteeism and presenteeism, as a proportion of the person's theoretical work hours and ranges from 0% to 100% (best to worst).

Statistical analysis

Descriptive statistics (mean, median, SD, range) were used to describe the overall distribution of clinical data and work outcomes from the population controls.

The proportion of controls with optimal outcomes (work ability=10 and at-work productivity loss=0%), as well as those with work impairment, was calculated and compared with that of iRMD patients, stratified by each age category (22–29, 30–39, 40–49, 50–59, 60–67).

Due to the excess of minimal or maximal scores in the outcomes (high percentage of individuals with perfect work ability (=10) and without productivity loss (=0%)) a zero-one-inflated beta (ZOIB) distribution was selected for further modelling. This is in line with published evidence showing that specifically modelling the zero inflation provides a better fit than traditional regression methods for this type of data.[22] Further, to deal with the bounded character of the variable (ie, having a clear upper and lower bound), the beta distribution was chosen to model values that do not belong to the excess zero or one part.

The association of potentially relevant CFs (age, sex, educational level, full-time or part-time employment and job demands) with each presenteeism instrument (work ability, productivity loss) was assessed through a generalised additive model for location, shape and scale parameters (GAMLSS)[22] to be able to model the (complex) ZOIB distribution. This analysis was intended to identify factors influencing the WP outcomes (p value <0.05) that would eventually need to be taken into account in the development of the RIs. Contrary to a regular linear regression or generalised linear models that assume linearity or certain type of distribution from the exponential family (respectively), GAMLSS allows to incorporate smoothing functions (eg, splines, fractional polynomials) when the model has a very non-linear distribution. Further, GAMLSS allow to model not only the mean of the distribution, but also the variance and shape and scale parameter, needed when modelling a complex distribution like the ZOIB distribution.[22]

GAMLSS was also used to establish age-specific RIs and percentile curves in the population of controls, and separate reference curves were computed for subgroups according to CFs with a relevant influence. An equation best fitting the data was derived for each outcome. When comparing different options for smoothing functions (cubic splines, natural splines and P-splines as a function of age), these did not improve the model fit or interpretation of the percentile curves, and therefore all models were fitted without any smoothing function. The percentile curves visualise the distribution of each of the outcome variables as a function of age as the continuous variable, with the age-specific 2.5th, 10th, 25th, 50th, 75th, 90th and 97.5th having been computed. To compare and identify the best model, the generalised Akaike information criterion (GAIC) was used. Generally, to avoid too complex models or overfitting, the model with the smallest GAIC-value was preferred. Missing data in the independent variables was handled using multiple imputations by fully conditional specification.

The number and proportion of controls and patients with iRMDs with the three outcomes under each percentile and stratified by each age category were tabulated.

All analyses were performed using R software, V.4.3.1.[23]

Table 2 Population controls and iRMDs patients with optimal outcomes

Age range	Total		Work ability=10 (100th percentile)		At work productivity loss=0% (0th percentile)		Overall productivity loss=0% (0th percentile)	
	Controls*	iRMDs	Controls n (%)	iRMDs n (%)	Controls n (%)	iRMDs n (%)	Controls n (%)	iRMDs n (%)
≥22 to <30	11–12	7	6 (50)	1 (14)	11 (100)	6 (86)	11 (100)	5 (71)
≥30 to <40	19–22	35	12 (55)	11 (31)	17 (77)	23 (65)	13 (68)	21 (60)
≥40 to <50	72–74	97	35 (47)	33 (34)	64 (86)	65 (67)	58 (81)	60 (62)
≥50 to <60	151–155	210	63 (42)	62 (30)	124 (80)	115 (55)	114 (75)	101 (48)
≥60 to <67	130–133	174	53 (40)	49 (28)	112 (84)	102 (59)	94 (72)	94 (54)
Total	383–395	523	169 (43)	156 (30)	328 (83)	311 (59)	290 (74)	281 (54)

*The number of controls with available data varied across the three work outcomes.
iRMDs, inflammatory rheumatic and musculoskeletal diseases.

RESULTS

A total of 413 controls and 903 iRMDs patients were included: mean age of participants was 53.5 (SD 9.9) and 53.2 (9.9) years for each group, 307 (74%) and 568 (63%) were female and the proportion of persons with high education was 60% and 55%, respectively. The mean work ability for controls and iRMDs was 8.7 (1.6) versus 8.1 (2.0), at-work productivity loss 7.5% (19.0) versus 16.6% (24.8) and overall work productivity loss 12.3% (27.0) versus 23.1 (31.8), respectively. The population characteristics and work outcomes are presented in table 1.

When considering optimal outcomes (work ability=10 and at-work/overall productivity loss=0) in iRMDs patients and population controls (table 2), it can be seen that iRMDs patients were less likely to have optimal work ability (n=156 (30%) vs n=169 (43%) in population controls) or no at-work/overall productivity loss (n=311 (59%) and 281 (54%) in patients vs n=328 (83%) and 290 (74%) in population controls). Furthermore, the gap between the population controls and iRMD patients was larger for at-work and overall productivity scores (24% and 20%, respectively) than for the work ability scores (13%), and this held for each age category.

Age-specific RIs

For the development of RIs, an equation best fitting the data was derived for each outcome (online supplemental text S1). From those equations, RIs can be computed for any age, and examples were chosen for the 22–29, 30–39, 40–49, 50–59 and 60–67 age ranges, for which several percentiles are indicated (eg, 50th, 25th, 10th and 2.5th for work ability—table 3). Age-specific percentiles for each outcome, as well as the number and proportion of population controls and patients with iRMDs under each percentile and for each age category for each of the three outcomes, are presented in tables 3–5 and figure 1A–C.

For work ability (table 3 and figure 1A), only the 2.5th, 10th, 25th and 50th percentiles are given since higher percentiles were all at the maximum work ability of 10 and no increase was seen in the percentage of persons. The same applies for at-work productivity loss (table 4 and figure 1B) and overall work productivity loss (table 5 and figure 1C), where only the 75th, 90th and 97.5th percentiles are given. For instance, for an individual aged between 22 and 30 years old, the 2.5 percentile for *work ability* was 5.9–10, which means that 2.5% of the population controls within this age range would be expected at or below the value 5.9. On the other hand, the 50th percentile was 10, meaning that 50% of the individuals in that age range would be expected to have optimal work ability. Similarly, but in the opposite direction, for the same individual, the 97.5% RI *for at-work productivity loss* was 0%–47.2%, therefore at-work productivity loss below that number would be expected in 97.5% of the population, or in other words, only 2.5% of them would have a productivity loss above 47.2%. In the other extreme, the 75% RI equalled a score of zero at-work productivity loss, meaning that 75% of the individuals in that age category would likely not have productivity loss. Finally, for *overall productivity los*s, using a different age range, for an individual from the control population between ≥40 and <50 years old, the 97.5% RI was 0%–75.9%, and therefore it can be said that a person belonging to the top 2.5% of the population from that age category would have an overall productivity loss higher than 75.9%.

In addition to the RIs and percentile curves derived from the population controls, the values reported by patients with iRMD were also plotted to allow their comparison with the percentile curves from the population controls.

Stratifying for education

When exploring the role of CFs, only the variable *education* (high vs low/middle education) was found to be potentially clinically relevant for all outcomes (online supplemental file 1). Therefore, in addition to the main analysis, separate curves were constructed stratified by educational level. The percentile curves for *work ability* based on the high-educated controls (60%) have a similar

Table 3 Reference intervals for work ability. Number and proportion of population controls and iRMDs patients with a work ability score under certain percentile*, for each age category

			50th percentile†			25th percentile			10th percentile			2.5th percentile		
Age range	Controls n=390	iRMDs n=523	Score	Controls n (%)	iRMDs	Score	Controls n (%)	iRMDs n (%)	Score	Controls n (%)	iRMDs n (%)	Score	Controls n (%)	iRMDs n (%)
22–29	12	7	10	12 (100)	7 (100)	7.9	3 (25)	5 (38)	6.9	1 (8)	3 (43)	5.9	0 (0)	2 (29)
30–39	22	35	9.7	10 (45)	24 (69)	7.8	4 (18)	12 (32)	6.8	1 (5)	3 (9)	5.6	0 (0)	3 (9)
40–49	74	97	9.3	39 (53)	64 (66)	7.7	13 (18)	36 (29)	6.6	4 (5)	14 (14)	5.3	4 (5)	9 (9)
50–59	151	210	9.1	88 (58)	148 (70)	7.6	27 (18)	64 (29)	6.3	15 (10)	33 (16)	5.0	4 (3)	10 (5)
60–67	131	174	9.1	78 (60)	125 (72)	7.5	26 (20)	44 (35)	6.1	12 (9)	35 (20)	4.6	4 (3)	13 (7)

Reference intervals scores were calculated for one specific age among the range.
*The lower the work ability score, the worse the work ability, so an average individual person with a score under a certain percentile (eg, 2.5th percentile) has a worse work ability than an (average) individual with a score just under a higher percentile (eg, between 5th and 10th percentile).
†Also included the 75th, 90th and 97.5th percentile.
iRMDs, inflammatory rheumatic and musculoskeletal diseases.

Table 4 Reference intervals for at-work productivity loss. Number and proportion of population controls and iRMDs patients with at-work productivity loss score under certain percentile* (ie, less at work productivity loss), for each age category

			75th percentile†			90th percentile			97.5th percentile		
Age range	Controls n=395	iRMDs n=523	Score	Controls n (%)	iRMDs	Score	Controls n (%)	iRMDs n (%)	Score	Controls n (%)	iRMDs n (%)
22–29	11	7	0.0	11 (100)	6 (86)	22.7	11 (100)	6 (86)	47.2	11 (100)	6 (86)
30–39	22	35	0.0	17 (77)	23 (66)	26.9	18 (82)	27 (77)	51.4	22 (100)	34 (97)
40–49	74	97	0.0	64 (86)	65 (67)	31.4	67 (91)	73 (75)	57.2	73 (99)	96 (99)
50–59	155	210	0.0	124 (80)	115 (55)	36.5	136 (88)	158 (75)	64.8	148 (95)	200 (95)
60–67	133	174	0.0	112 (84)	102 (59)	42.2	122 (92)	138 (79)	75.1	131 (98)	167 (96)

Reference intervals scores were calculated for one specific age among the range.
*The higher the productivity loss score, the higher the productivity loss, so a(n) average) person with a score above a certain percentile (eg, 97.5th percentile) reflects a worse productivity work than a(n) average) person with a score above a lower percentile (eg, 75th percentile).
†Also included the 50th, 25th,10th and 2.5th percentile.
iRMDs, inflammatory rheumatic and musculoskeletal diseases.

Table 5 Reference intervals for overall productivity loss. Number and proportion of population controls and iRMDs patients with overall work productivity loss score under certain percentile*, for each age category

Age range	Controls n=383	iRMDs n=523	75th percentile† Score	Controls n (%)	iRMDs	90th percentile Score	Controls n (%)	iRMDs n (%)	97.5th percentile Score	Controls n (%)	iRMDs n (%)
22–29	11	7	0.0	11 (100)	5 (71)	41.2	11 (100)	6 (86)	69.8	11 (100)	7 (100)
30–39	19	35	0.0	13 (68)	21 (60)	45.3	17 (88)	30 (86)	71.6	19 (100)	33 (94)
40–49	72	97	0.0	58 (81)	60 (62)	50.4	68 (94)	88 (91)	75.9	70 (97)	93 (96)
50–59	151	210	3.2	114 (75)	101 (48)	58.3	135 (89)	175 (83)	95.2	144 (95)	194 (92)
60–67	130	174	35.2	98 (75)	113 (65)	82.4	119 (92)	157 (90)	100	130 (100)	174 (100)

Reference intervals scores were calculated for one specific age among the range.
*The higher the productivity loss score, the higher the impairment, so an individual's score above a certain percentile (eg, 97.5th percentile) has worse productivity work than an individual with a score above a lower percentile (eg, 75th percentile).
†Also included the 50th, 25th, 10th and 2.5th percentile.
iRMDs, inflammatory rheumatic and musculoskeletal diseases.

behaviour to the total population controls (figure 2A) while the curves for the lower/middle-educated controls (40%) seem to have an increase in variability around the work ability scores for higher ages (figure 2B). The percentile curves for *productivity loss* stratified by education (figure 2C–F) show that in the lower educated controls, the worsening (at-work and overall productivity loss) seems to start at lower age.

Work ability and work productivity loss in patients compared with population controls

Tables 3–5 also present the number and proportion of iRMDs patients and controls within different age categories below each percentile curve for work ability or above each percentile curve for the productivity loss outcomes. As expected, the proportion of patients with lower work ability was almost consistently higher compared with controls and this was true for almost all percentiles and age categories. For example, among those between 40 and 49 years old, there were four (5%) individuals from the control group versus nine (9%) iRMDs patients below the 2.5th percentile and experienced maximal inability to work (table 3). Similarly, the proportion of iRMD patients reporting limited at-work and overall productivity loss was higher compared with the controls (tables 4 and 5).

DISCUSSION

In the present study, age-specific percentile curves for work ability, at-work productivity loss and overall work productivity were constructed for population controls to use as benchmark when interpreting work outcomes of patients with iRMDs. These curves confirm that work outcomes in the general population are not always optimal nor static, with a natural course of worse outcomes with increasing age.

To our knowledge, this is the first study constructing percentile curves for work outcomes from a general population sample. The development of these age-specific RIs describing the natural course of WP across individuals with no chronic physical health impairment allows for a more accurate assessment than just the mere comparison between the mean and SD of a certain outcome variable. RIs and percentile curves are easier to interpret than other summary statistics, even for people without strong statistical background, probably due to the familiarity with the very widespread percentile growth curves from paediatrics. This has a large value for researchers in the field of RMDs or other chronic diseases, who can now easily extrapolate the natural process of ageing on work ability and productivity (toward its normality ranges) to affected patients. As it has been shown that these outcomes are strong predictors of long-term sickness absence and withdrawal from the work force, the measure will be increasingly used in practice to signal these persons that require additional support towards sustainable participation.

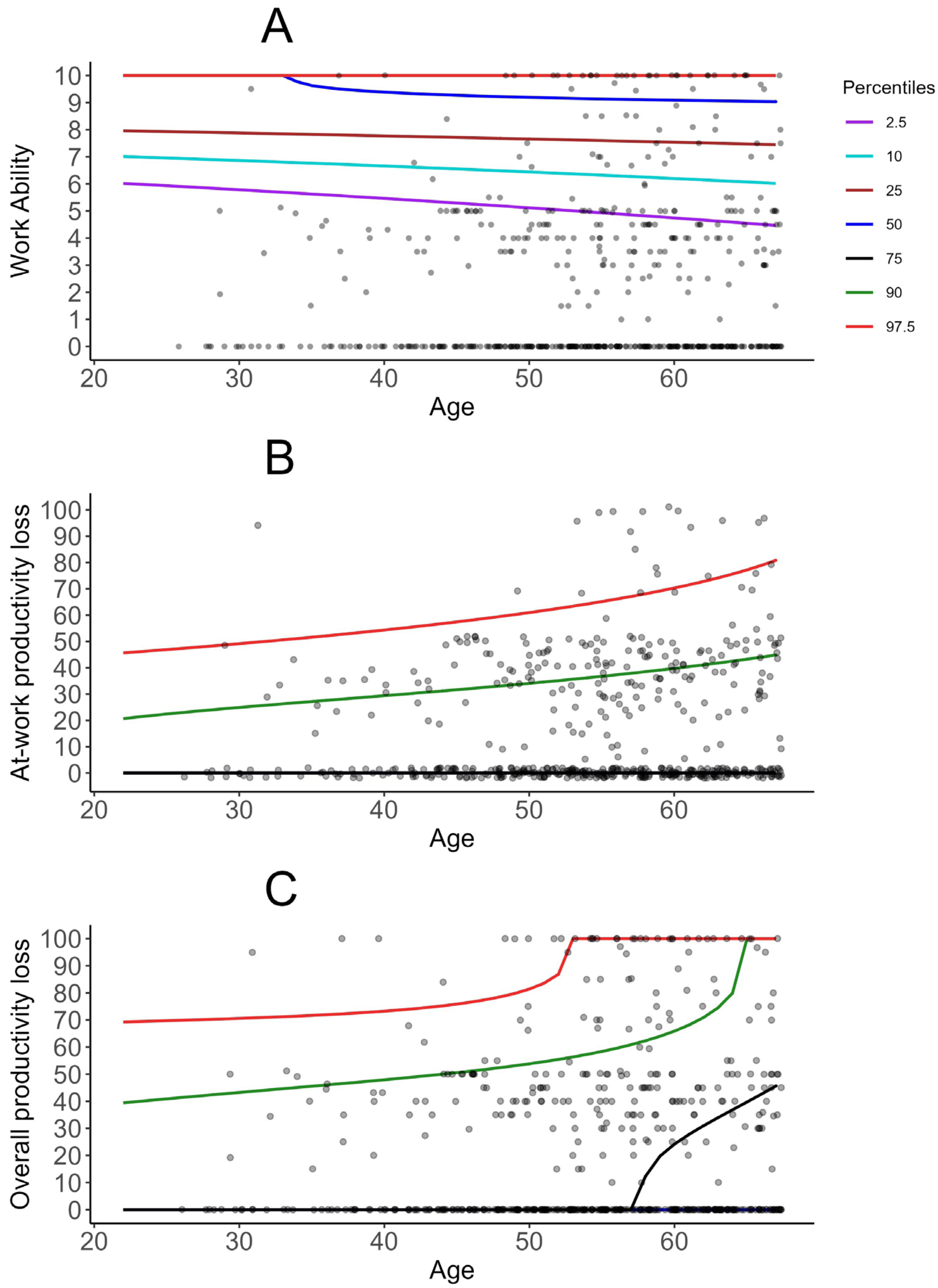

Figure 1 Reference intervals and percentile curves for the general population for (A) work ability, (B) at-work productivity loss at work and (C) overall work productivity loss.

These percentile curves showed that the majority of the population controls (over 75%) do not experience any at-work or overall productivity loss. On the contrary, more than 50% of the population controls older than 30 years report at least some impairment in work ability. This shows that without the construction of these curves for population controls, the impact of iRMDs on the limitations in work ability and work productivity would indeed be overestimated if the benchmark would be set at on a perfect score.

However, the applicability of these curves and especially the question what constitutes 'normal' work outcomes might not be straightforward. One proposal could be to choose a score indicating severe impairment in work outcomes, like the 2.5th percentile for work ability or the 97.5th for productivity loss. This would apply in a normal distribution considering a total of 5% with 'abnormal' values, namely 2.5% of the patients with a lower value and 2.5% of the patients with a higher value. Nevertheless, this is a strict approach, only identifying a clear minority of the potentially problematic cases. Another possible scenario of taking the median percentile of the population controls as a benchmark would not solve the limitation. Alternatively, one could select a cut-off to define 'abnormality' based on trade-off between sensitivity and specificity of percentile lines on an external

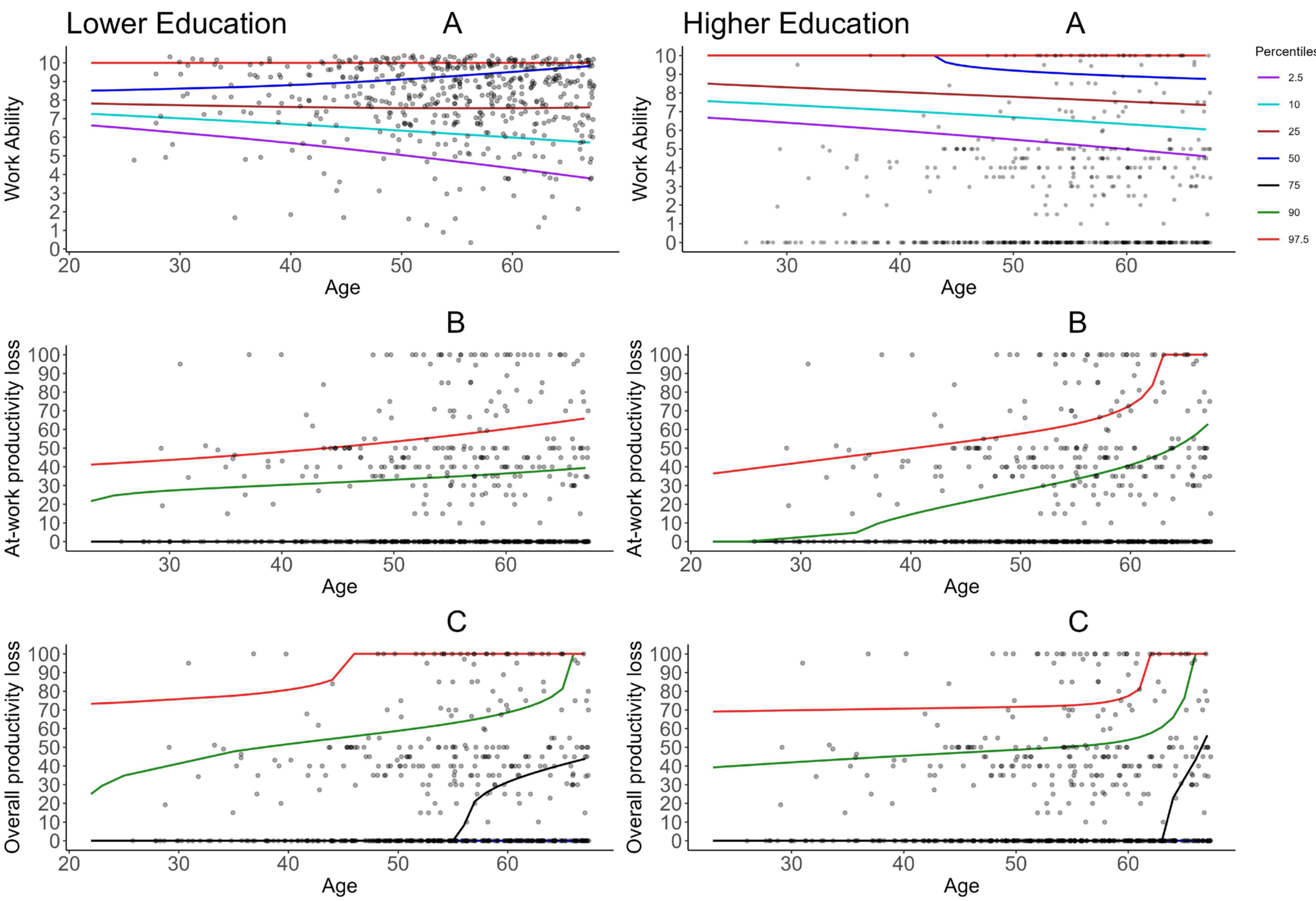

Figure 2 Reference intervals and percentile curves general population for work ability, at-work productivity loss and overall work productivity loss in lower educated (left) versus higher educated (right) population controls. *Dots in the figures represent patients.

outcome such as the risk of withdrawal from labour force. A final and more comprehensive solution is to use the percentile curves as a whole instead of trying to find one benchmark to compare the individual patient's results with. As previously said, variation in potential applications is widespread and with a known use through the growth curves used in paediatrics, where these growth references are used to screen and monitor growth in individuals and populations.[24] Nevertheless, the major difference between them is that, at the moment, these newly developed curves are mainly intended for gaining insight into groups of patients, rather than individual trajectories. Additionally, since they were developed with cross-sectional data, they are not intended for longitudinal use without first testing it. In rheumatology, there is a precedent of these kind of percentile curves, since spinal mobility curves in healthy individuals were developed for application in individuals with impaired axial mobility, such as patients with axial spondyloarthritis.[25–28] In these situations, impaired spinal mobility has also been defined as a spinal mobility measure below the 2.5th or the 5th percentile. A similar use can be expected for the definition of impaired work outcomes (for some outcomes, defining an impaired outcome as above for example the 95th percentile), and the detailed explanation of online supplemental text S1 can assist the calculation of the impaired outcomes, making their use in future studies more straightforward and feasible.

It is evident that age is an important CF of work impairment.[29–32] Accordingly, the computation of the percentile curves was age-specific. Regarding the other CFs evaluated in the present study, only educational level was found to be associated with the three outcomes. In line with our analysis, although lower educational levels are generally associated with more physically demanding jobs, a previous study also found that despite lower-educated employees having more unskilled occupations, education remained as an associated factor whereas physically demanding job did not, after the appropriate adjustments were made.[30] In our analysis, a higher variability was found in the work ability curves from the lower/middle-educated population controls (worse as well as better scores in small proportions of the older, compared with younger controls). However, it is uncertain to what extent this reflects larger heterogeneity of the construct 'education' among older persons (with stronger influence of self-management skills, coping or other socioeconomic factor) or methodological bias (the small number of patients, or a stronger healthy worker effect on work ability in lower educated persons) that could explain this heavily skewed distribution. This analysis should be replicated in a larger population, also taking into account younger persons, before stating the need for stratified curves or whether the overall curves would perform well enough.

Finally, when comparing outcomes between controls and patients across percentiles, differences were larger for work productivity than work ability independently of age. In other words, the impact of an iRMD on WP seems stronger on productivity than on work ability. Apparently, persons without chronic iRMD can have more physical and mental reserve to compensate their productivity despite reduced work ability. Clearly, the current analyses confirm that ability (difficulty) and productivity (output) are aspects of the same outcome (presenteeism).

The main limitation of this study is its cross-sectional design, which impairs a conclusion on the evolution of work outcomes within one person with increasing age. A longitudinal study in the general population could give more insights into the evolution of the work ability and productivity scores over time. Moreover, as a recurrent issue when studying work outcomes, the extrapolation of the percentile curves to other countries with different employment rights needs to be made with caution. From a statistical perspective, the first challenge we encountered was the high number of individuals with minimal or maximal scores (no work productivity loss and perfect work ability), which led to a high risk of underestimating these scores (0 or 1). However, this issue was resolved by using the ZOIB model, which effectively handles the bounded distribution of scores as well as overdispersion due to an excess of minimal or maximal scores. Finally, although data collection for the cohort started early after the onset of the COVID-19 pandemic, the work-related data used here was from the assessment during the post-pandemic period (March 2022), when life had largely returned to a 'new normal'. This timing makes it more representative of the current work environment. Additionally, previous analyses in this cohort showed a low frequency of COVID-19-related adverse work outcomes in both control and patient groups.[19]

On the other hand, one of the main strengths of this study is the fact that the WP percentile curves were developed in a general population sample and therefore they can be used not only as a benchmark for iRMDs patients but can be also applicable to patients with other chronic diseases.

In summary, this study demonstrates that work ability and productivity are not optimal in the general working population, suggesting that we should be cautious to not overestimate the impact of iRMD on presenteeism. For the first time, age-specific percentile curves and RIs have been developed to understand the effect of ageing on work outcomes and to reduce the risk of overestimating work outcome impairments in patients with iRMDs and other chronic diseases. Nevertheless, iRMDs have a significant impact on presenteeism compared with population controls, with this effect being stronger on productivity (output) than on ability (difficulty).

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