Doctoral School of Business and Management

Ph.D. Dissertation

Omar Alrashdan

Transferability of Productivity Loss Costs in Non-Communicable Diseases: Local Factors and Regional Adjustments

Supervisors: Prof. Valentin Brodszky, MD, Ph.D., Habil.

Dr. Zsombor Zrubka, MD, MBA, Ph.D.

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Corvinus University of Budapest
Department of Health Economics

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I. BACKGROUND

I.1. Introduction

Productivity is a measure of output per unit of input (Zhang, Bansback, & Anis, 2011). In health sciences, productivity loss (PL) refers to the individual's forgone output due to a health issue corresponding to the reduced output compared to a healthy individual. Recent years have seen considerable attention towards the adoption of a societal perspective in health economic evaluations (Brennan, Perola, van Ommen, Riboli, & Consortium, 2017). The inclusion of the societal costs into health economic evaluations can better inform policy and health decision-makers toward maximising national social welfare, even if entry costs might fall outside the annual healthcare budgets (Krol & Brouwer, 2014).

Non-communicable diseases (NCDs) have been recognised to be one of the major challenges hindering countries face in their efforts to reach their sustainable development goals (SDG) (Horton, 2013). NCDs are chronic conditions requiring prolonged, expensive treatment regimens that adversely affect national revenue, socio-economic welfare, and economic growth, both directly (through medical and non-medical treatment costs) and indirectly due to productivity losses of patients as well as their carers (Bloom et al., 2012). This has been placing increasing pressure on policymakers to reimburse the most cost-effective health intervention while assuring future societal welfare.

While Health Technology Assessment (HTA) generally mandates a societal perspective for informing reimbursement and resource allocation decisions, the bulk of the health economic evaluations -which are building blocks of HTA- often adopt a narrow health system perspective. Productivity loss (PL) is simply defined as the forgone output due to health issues corresponding to the reduced output compared to a healthy individual, whether paid or unpaid (Zhang et al., 2011). The inclusion of the societal costs into health economic evaluations can better inform policy and health decision-makers toward maximising national social welfare, even if entry costs might fall outside the

annual healthcare budgets (Krol & Brouwer, 2014). Krol and Brouwer (2014) further demonstrated that productivity loss costs can potentially be higher than the associated direct medical costs.

The Middle east north Africa (MENA) region although comprising a variation in income levels, yet the region as a whole is suffering from typical LMICs symptoms of data, experts, and evidence scarcity (Ahmed M. Soliman, 2013; Al-Aqeel, 2012; Hammad, 2016). Although transferability of health economic evaluations can seem like a simple solution for the region, yet methodological diversity, non-standardisation as well as the specificities of each disease are some of the factors contributing to the complexity of the costs' transferability across countries. We chose to work specifically with the V4 given the converging local variances in income levels, reimbursement capacity as well as the recent experience of member countries in HTA development and institutionalization. We also use HTA as a proxy for the awareness level and progression towards the adoption of a societal perspective in reimbursement decisions.

I.2. Objectives

This work aims to demonstrate the socio-economic value of lost patients' productivity due to NCDs and provide a reference for future utilisation and transferability of PL costs from the V4 into the MENA region. Using HTA as a proxy we systematically explore the contrast in HTA scientific output between the MENA and Central and Eastern Europe (CEE). Our aims bifurcated later on given specific regional needs to reach our transferability aim.

Data scarcity from the MENA region dictated systematically mapping the health economic evidence allowing us to create a comprehensive MENA PL costs catalogue, facilitating assessment and transferability of PL costs. On the other hand, given the relative abundance of health economic research from the V4 region, we aimed to locally identify and rank NCDs PL impact as well as their significant PL drivers in order to be able to propose a simplified method for transferring PL cost estimates cross-regionally,

utilising economic indicators corresponding to our identified PL drivers. In each of the chapters, I contextualise the research goals based on previous work and literature in light of my aims. Figure 1 below illustrates the research framework adopted in this dissertation.

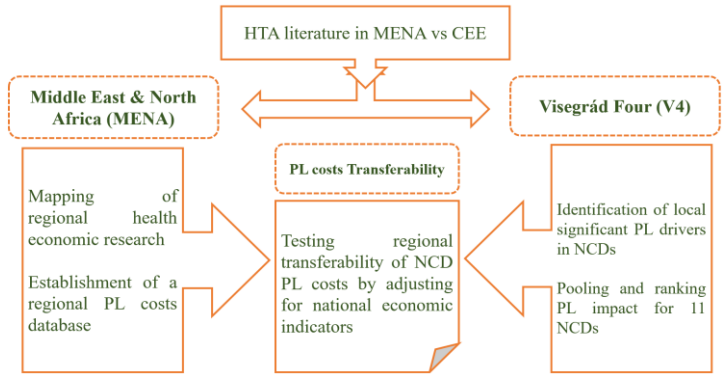

Figure 1. Dissertation's research framework.

II. HYPOTHESES

The following hypotheses were tested concerning each chapter's aim in light of our final goals:

- Hypothesis 1 (H1): Given the superior financial capacity in high-income countries, we assume that their group will comprise the highest share of full economic evaluations from the MENA region. (Rejected)

- Hypothesis 2 (H2): Among the MENA studies reporting societal perspective costs, we assume that there is a significant association between country income groups and investigated ICD-10 disease groups. (Accepted)

- Hypothesis 3 (H3): Health status and educational level are significant predictors for musculoskeletal disease PL costs. (Accepted)

- Hypothesis 4 (H4): We assume that cross-country PL cost differences are negligible among the V4, provided similar social and economic welfare. Hence, insignificant differences in PL cost estimates are expected within the region. (Accepted)

- Hypothesis 5 (H5): We assume that incorporating the national Human capital index (HCI) as an adjustment factor can aid in generating more precise PL estimates interregionally than sole GDP/capita adjustment. (Accepted)

- Hypothesis 6 (H6): we assume that adjusting for health expenditure (HE) as an adjustment factor can aid further in generating more precise international disease cost estimates when coupled with GDP/capita. (Rejected)

III. METHODS

III.1. HTA BETWEEN THE MENA AND CEE: A SCOOPING ANALYSIS OF LOCAL RESEARCH

Bibliometric analysis for high-quality peer-reviewed HTA research from the MENA and CEE using Scopus database R studio equipped with “bibliometrix” R-package was used to generate the scientific output per country, and SPSS 23 statistical software was used to test for significant SJR group mean differences.

III.2. HEALTH ECONOMIC RESEARCH FROM THE MENA REGION

Systematic review methodology was chosen as a regional literature analysis tool. MEDLINE (i.e. PubMed) was chosen as a source database, and PRISMA guidelines were followed in reporting our review. Health economic publications were identified by devising a comprehensive keyword search criterion based on similar methodological studies. We included comparison Journal articles reporting original research on humans, involved the local population from the target MENA countries, was a full or partial health economic analysis were included. For data extraction and descriptives, a Microsoft Excel spreadsheet was prepared; the first author's name, publication year, the target country, funding source, income status, the health technology under evaluation, the type of economic evaluation, the studies' perspective, and the Scimago journal rank. Fisher’s exact test was used to test our first hypothesis (H1).

III.3. PL COSTS FROM THE MENA: TOWARDS A REGIONAL PL CATALOUGE

In this chapter, we identified all health economic research reporting PL costs using our previous search code. However, we included studies not reporting a comparator as long

as they reported PL costs per patient per year, or can be calculated without modelling or complex calculations. To complete our domain, we checked and reviewed the papers included in the previous three high-quality regional reviews, consolidated, and compiled into one database to create our comprehensive regional PL costs catalogue. To test our second hypothesis (H2), Fisher's exact test was used for 2x2 tables while chi-squared test was used for larger tables, and Cramer V statistic was reported for significant associations.

III.4. PL FACTORS IN NCD PATIENTS: A POOLED ECONOMIC ANALYSIS

We started by collecting, translating, and compiling patient-level raw data on demographics, health-related quality of life, resource use, and productivity loss from eleven NCD non-interventional, cross-sectional, retrospective, COI studies conducted in different medical centres in Hungary between the years 2003-2015, involving the following eleven chronic diseases: psoriatic arthritis, benign prostatic hyperplasia (BPH), dementia, diabetes, epilepsy, multiple sclerosis, Parkinson's disease, psoriasis, rheumatoid arthritis, schizophrenia, and systemic sclerosis. Costs were adjusted for each disease to reflect the value in 2018-euro rates, and indirect costs were expressed as a percentage of GDP per capita (PL/(GDP/capita)). ANOVA analysis was used to compare disease group means of lost productive hours, while Spearman's rho was employed to identify significant correlations between the scale variables, and they were both used to test our third hypothesis (H3). Finally, four weighted linear regression models were built to predict significant PL drivers in our pooled sample.

III.5. REGIONAL ESTIMATES AND TRANSFERABILITY OF PRODUCTIVITY LOSS COSTS OF MUSCULOSKELETAL DISEASE: V4 TO MENA

In this chapter, we identify, pool, and normalise musculoskeletal disease PL costs from the V4 region, and we utilise the identified musculoskeletal PL cost drivers (education, and health) to adjust our PL estimates into the MENA region accordingly. Using our MENA PL catalogue as a reference, we test our musculoskeletal disease adjustments against Tunisia's reported absenteeism costs for musculoskeletal disease (Younes et al., 2010), using mean absolute differences (MADs) to measure accuracy and the standard error (SE) of means to measure each adjustment precision. While we used ANOVA to test our fourth hypothesis (H4), we used SE to test our fifth and sixth hypotheses (H5 and H6).

IV. RESULTS

IV.1. HTA BETWEEN THE MENA AND CEE: A SCOOPING ANALYSIS OF LOCAL RESEARCH

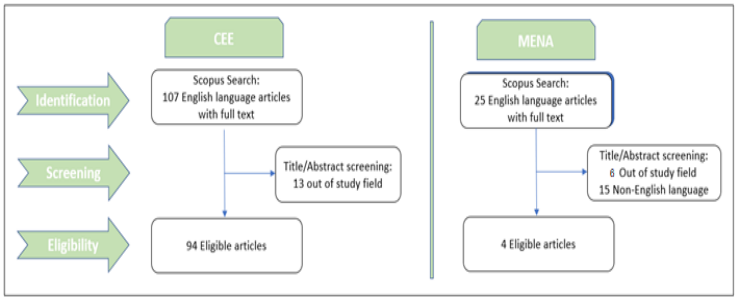

Figure 2. Prisma flow diagram for our CEE and MENA search.

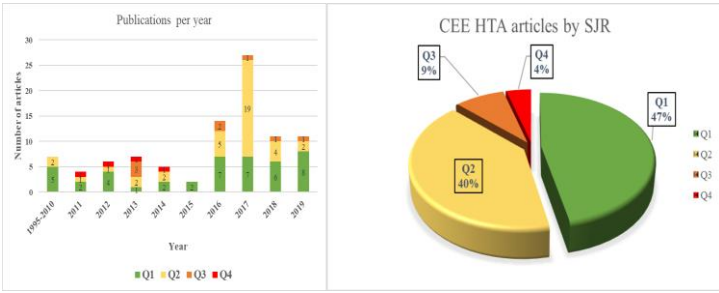

Figure 3. CEE HTA publications by year and SJR.

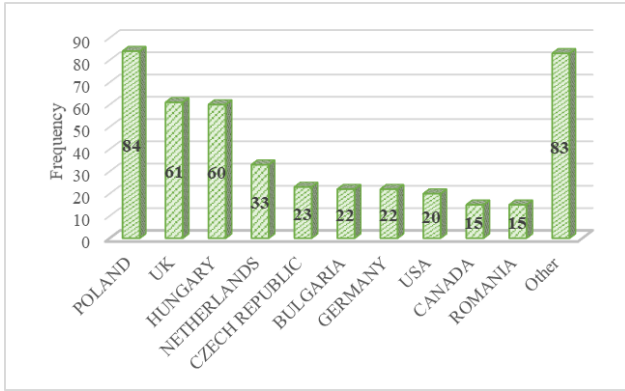

Figure 4. Scientific output of CEE by frequency of authors' affiliation country.

In our explorative analysis of HTA literature from the CEE and MENA regions, we observed that that the CEE countries have been progressing notably in the last 10 years while the MENA is still lagging far behind. This concludes that different health economic research contributions are needed for each region. Therefore, for the MENA region, we decided to dive deeper into the region's health economic evaluations, their types, quality, and active countries to identify the gaps in societal costs reporting. For the CEE region, we opted to narrow our source region into the V4 provided the relative concentration of HTA research output from the group, in addition to their similar political and economic states which should contribute to minimising interregional costs bias. In the following two chapters (V and VI) we proceed with the mapping of MENA health economic research to create a PL costs library for transferability facilitation.

IV.2. COMPARATIVE HEALTH ECONOMIC RESEARCH FROM THE MENA REGION

Our search order resulted in 2017 hits, went down to 1646 after applying English language and full-text filters. Screening by title/abstract resulted in 219 articles eligible for full-text assessment. From those, we excluded 114 articles to reach our final number of articles eligible for our analysis n=105 articles.

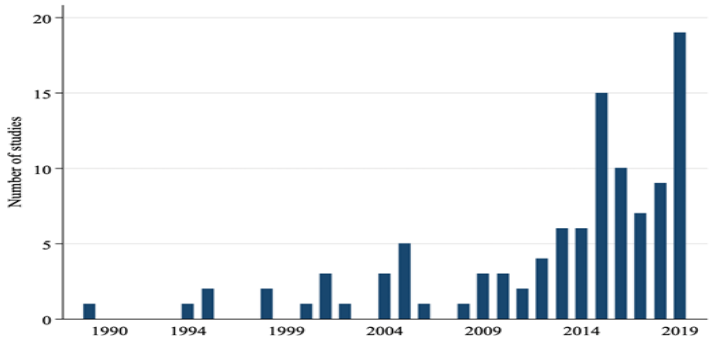

Figure 5. Number of comparative health economic studies by publication year from the MENA.

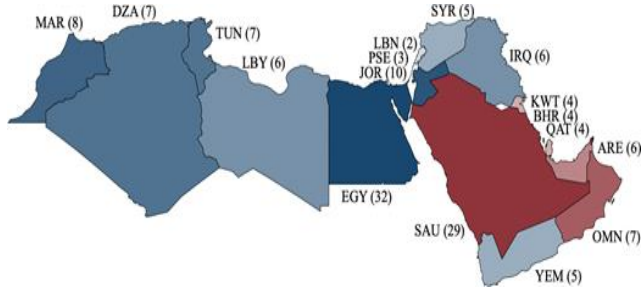

Figure 6. Gradient MENA map presenting the number of analyses per country.

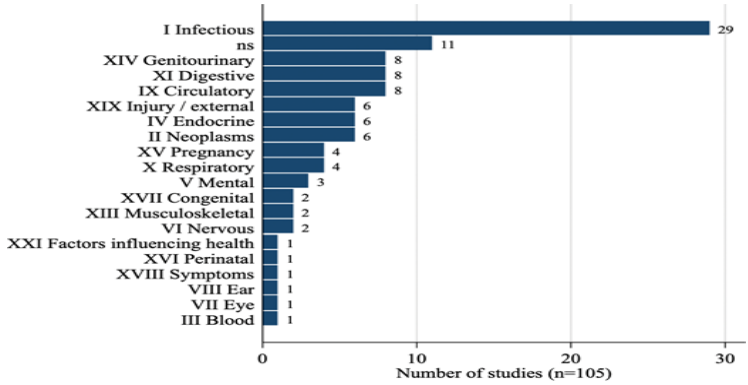

Figure 7. Number of comparative health economic studied from the MENA by ICD-10 disease area.

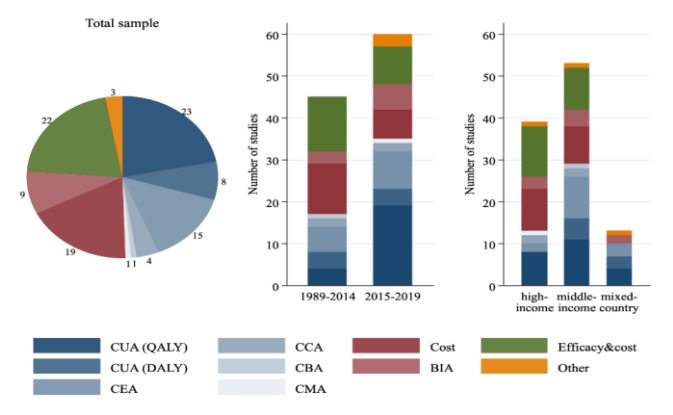

Figure 8. Number of comparative health economic studies by type of economic evaluation.

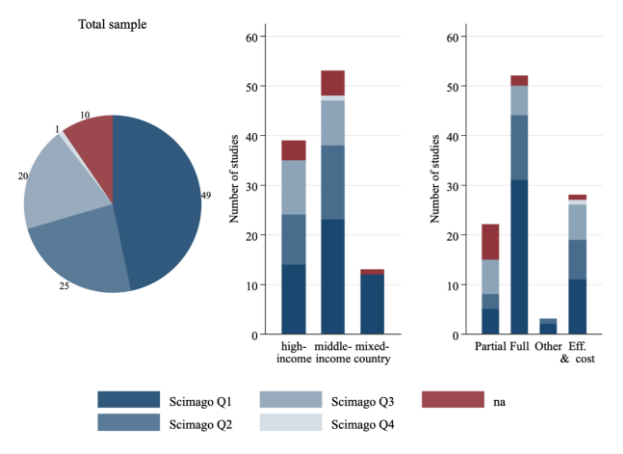

Figure 9. Number of comparative health economic studies stratified by SJR, type of evaluation, and country income level.

This scoping review is the largest account of comparative health economic evaluations for the MENA region. The 105 identified evaluations, their targeted countries, diseases, technologies, and methods in addition to their bibliometric properties were analysed. Significant growth in the publications started emerging after 2014 given that more than half of the evaluations were published in the past 5-6 years. A total of 145 country-specific results were identified, of which the majority were from middle-income countries rather than high-income countries. Almost half of the studies were full economic evaluations in which the health system was the predominant perspective. The proportion of full economic evaluations was significantly greater in middle-income compared to high-income countries (Fischer's exact test, $p = 0.04$), leading us to reject our first hypothesis (reject H1). Infectious disease was the top investigated ICD-10 disease group in the region. Differences in health economic research orientation were significant among income groups as the majority of studies on infectious diseases originated from middle-income countries.

Public health priorities in the region as reported by The World Bank concluded almost two decades ago that musculoskeletal and mental disease were among the top five leading causes of disability in the region, yet our results show that those two disease groups were respectively at the 12th and 10th place among the overall studied disease areas in the region. Out of diverging priorities from recommendations, the importance of assessing NCDs' societal burden for the region can be of significant value in light of such specific scarcity in the region’s health economic literature. Provided the limited availability of indirect cost estimates, we proceed with creating a regional catalogue for PL costs to aid in future transferability efforts.

IV.3. PL COSTS FROM THE MENA: TOWARDS A REGIONAL PL CATALOUGE

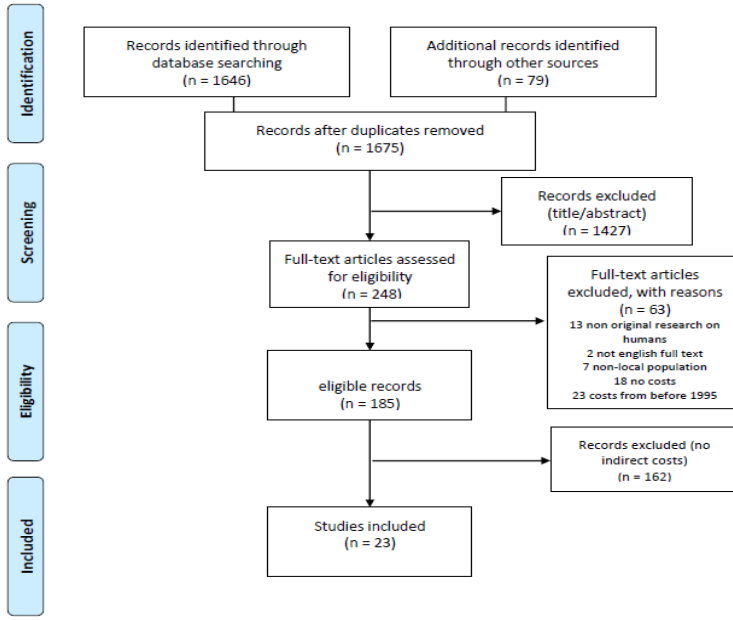

Figure 10. Prisma flowchart for MENA PL costs identification.

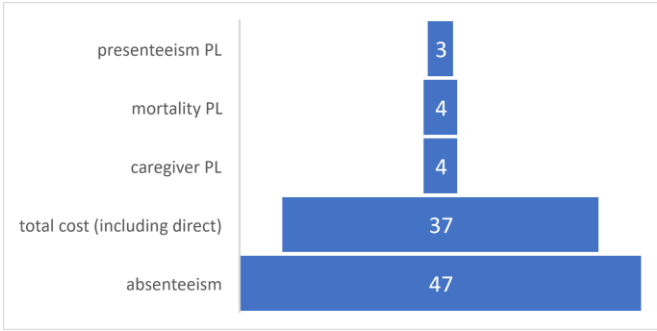

Figure 11. funnel chart of MENA PL cost items by type.

This chapter presents the largest pooling of disease PL costs from the MENA region. We extracted, categorised, and mapped out the regions' PL costs to facilitate future field research, and boost transferability efforts in the region. We found a significant association ($p<0.000$) between country income groups and the investigated ICD-10 disease chapters, with a high association level (Cramer's $V=0.808$) leading us to accept our second hypothesis (accept H2). In light of reported PL costs distribution, although diseases of the musculoskeletal system were third in line after infectious and respiratory diseases in terms of reported PL costs count, yet only one study reported indirect costs for musculoskeletal disease from the MENA. In such mobility limiting diseases, the social impact is undeniable on both the patient and the caregiver. Scarce efforts have been shown in the region to address musculoskeletal disease and its societal cost. Our review has concluded sufficient PL costs from the musculoskeletal disease chapter to test for our transferability hypotheses. But first, we steer our direction towards the identification of local significant demographic, health status, and utility factors impacting PL costs in an attempt to develop an understanding of PL determinants on a microeconomic level to aid in our regional PL costs transferability adjustments.

IV.4. PL FACTORS IN NCD PATIENTS: A POOLED ECONOMIC ANALYSIS

Table 1. Disease-specific demographics, annual resource use, health status, adjusted indirect cost, and indirect cost as a percent of the total cost.

Disease name	Total number of patients	Number of patients below 64	Age mean (95% C.I.)	Higher education patients N (%)	Females N (%)	EQ-5D-3L Index (95% C.I.)	Disease duration in years (95% C.I.)	Number of outpatient visits mean (95% C.I.)	Number of GP visits mean (95% C.I.)	Number of hospital admissions mean (95% C.I.)	Number of missed working hours per year mean (95% C.I.)	Adjusted indirect (PL) cost in Euros (2018 rates)	Adjusted total cost in Euros (2018 rates)	Indirect (PL) Cost as a percent of total cost
Benign prostatic hyperplasia	246	49	70.59 (69.56, 71.61)	74 (30%)	0 (0.0)	0.85 (0.83, 0.88))	5.56 (4.95, 6.18)	6.60 (5.63, 7.57)	1.04 (0.63, 1.45)	1.08 (0.97, 1.19)	35.67 (7.42, 63.92)	213.01, (44.28, 381.74)	917.21, (676.65, 1157.46)	23.2%
Dementia	88	6	77.55 (75.75, 79.37)	12 (14%)	52 (59.1)	0.39 (0.32, 0.46)	4.32 (3.11, 5.53)	1.15 (0.85, 1.44)	0.85 (0.64, 1.07)	0.11 (0.05, 0.18	104.65 (29.26, 180.04)	624.51, (174.61, 1074.40)	4159.21, (2490.39, 5828.03)	15.0%
Diabetes	480	331	52.56 (51.08, 54.05)	N/A	267 (55.6)	0.77 (0.74, 0.79)	15.60 (13.72, 15.48)	5.45 (5.02, 5.88)	7.29 (6.69, 7.89)	N/A	187.99 (138.04, 237.94)	1121.2, (823.31, 1419.11)	2433.36, (2130.67, 2736.07)	46.1%
Epilepsy	100	97	36.65 (34.16, 39.14)	18 (18%)	58 (58.0)	0.78 (0.74, 0.86)	15.45 (13.04, 17.87)	3.52 (2.63, 4.41)	3.27 (2.25, 4.28)	0.44 (0.11, 0.76)	214.96 (135.62, 294.29)	1283.94, (810.05, 1757.79)	2617.55, (1920.52, 3314.57)	49.1%
Multiple sclerosis	68	67	37.96 (35.74, 40.17)	28 (42%)	48 (70.6)	0.67 (0.60, 74)	7.02 (5.55, 8.48)	3.02 (2.16, 3.87)	1.33 (0.80, 1.86)	0.49 (0.32, 0.65)	403.61 (225.93, 581.28)	2422.67, (1349.48, 3495.85)	11786.35, (9980.34, 13592.36)	20.6%
Parkinson's disease	110	55	63.28 (61.15, 65.41)	40 (36%)	36 (32.7)	0.58 (0.52, 0.65)	8.22 (7.10, 9.33)	4.86 (3.77, 5.96)	3.22 (2.41, 4.03)	0.42 (0.28, 0.55)	381.20 (227.21, 535.20)	2276.91, (1357.12, 3196.69)	6518.57, (5348.36, 7788.8)	34.9%
Psoriasis	200	157	50.66 (48.83, 52.50)	40 (20%)	64 (32.0)	0.69 (0.65, 74)	21.44 (19.80, 23.08)	1.61 (1.24, 1.98)	4.26 (3.05, 5.47)	1.72 (1.65, 1.78)	206.4 (126.8, 286.0)	1231.85, (756.86, 1706.85)	8728.09, (7305.24, 9950.93)	14.1%
Psoriatic arthritis	183	149	50.15 (48.25, 52.04)	43 (24%)	105 (57.4)	0.47 (0.42, 52)	9.24 (7.89, 10.59)	6.38 (5.25, 7.52)	3.70 (2.87, 4.54)	0.64 (0.51, 0.78)	505.21 (380.88, 629.55)	3015.11, (2273.13, 3757.08)	5787.76, (4644.17, 6931.34)	52.1%
Rheumatoid arthritis	255	182	55.45 (53.93, 56.97)	42 (17%)	218 (85.5)	0.46 (0.42, 0.50)	9.10 (7.92, 10.27)	7.78 (6.87, 8.70)	8.99 (8.11, 9.87)	1.09 (0.93, 1.25)	1636.69 (1389.78, 1883.59)	9768.06, (8290.25, 11235.86)	14489.14, (12877.05, 16101.24)	67.4%
Schizophrenia	78	73	44.24 (41.30, 47.19)	9 (12%)	36 (46.2)	0.64 (0.57, 0.71)	N/A	14.91 (11.26, 18.56)	1.76 (0.57, 2.94)	N/A	1659.56 (1474.66, 1844.46)	9912.5, (8808.1, 11016.22)	15003.52, (13308.88, 16698.17)	66.1%
Systemic sclerosis	80	56	57.39 (55.25, 59.52)	16 (20%)	72 (90.0)	0.58 (0.52, 0.64)	7.16 (5.68, 8.64)	7.14 (5.44, 8.85)	10.26 (8.92, 11.60)	4.61 (3.94, 5.29)	1023.02 (789.94, 1256.11)	6103.74, (4713.06, 7494.42)	10893.16, (9289.18, 12217.12)	56.0%
Total	1888	1222	55.17 (54.44, 55.91)	956 (50.6)	0.66 (0.64, 0.67)	11.40 (10.92, 11.88)	5.64 (5.32, 5.97)	4.74 (4.44, 5.04)	1.15 (1.06, 1.25)	509.32 (460.06, 558.59)	2464.03, (2243.12, 2684.95)	5684.59, (5338.09, 6031.1)	43.3%

Table 2. Disease-specific drivers of PL (hours lost/year) with demographics, resource use, and health status indicators.

Disease Name	Correlation with lost productive hours						Gender		Education		Informal care	
	GP visit	Hospital admissions	Outpatient visits	EQ-5D-3L Index	Age (all)	Age (<64)	Female (Male)	P	Higher (Lower)	P	Received (Did not receive)	P
	Spearman's rho (P)						Lost hours mean	ANOVA	Lost hours mean	ANOVA	N (%)	ANOVA
Benign Prostatic Hyperplasia	-0.027 (0.677)	**0.962 (0.000)**	-0.010 (0.881)	0.116 (0.074)	**-0.321 (0.000)**	-0.107 (0.465)	N/A 35.67	N/A	**78.71 (17.25)**	**0.050**	0.0 (38.15)	0.513
Dementia	-0.001 (0.990)	**0.275 (0.010)**	0.082 (0.447)	-0.074 (0.495)	0.118 (0.276)	N/A*	136.88 (59.76)	0.327	26.50 (116.99)	0.416	120.83 (13.35)	0.358
Diabetes	0.040 (0.416)	N/A	-0.085 (0.064)	**-0.232 (0.000)**	0.001 (0.985)	**0.133 (0.014)**	**131.17 (259.12)**	**0.012**	N/A	N/A	N/A	N/A
Epilepsy	0.203 (0.073)	0.199 (0.068)	**0.197 (0.050)**	**-0.531 (0.000)**	**0.448 (0.000)**	**0.488 (0.000)**	**282.62 (121.52)**	**0.046**	64.94 (247.89)	0.079	**739.62 (118.55)**	**0.000**
Multiple sclerosis	0.240 (0.051)	**0.428 (0.000)**	0.219 (0.079)	**-0.306 (0.011)**	0.231 (0.060)	0.231 (0.060)	416.13 (380.36)	0.858	250.33 (474.17)	0.211	**856.11 (143.69)**	**0.000**
Parkinson's Disease	0.234 (0.14)	**0.207 (0.030)**	0.066 (0.492)	-0.141 (0.160)	**-0.567 (0.000)**	**-0.421 (0.001)**	366.97 (385.72)	0.911	277.38 (440.53)	0.315	522.24 (254.76)	0.086
Psoriasis	-0.011 (0.873)	**-0.256 (0.000)**	0.049 (0.498)	-0.112 (0.121)	-0.137 (0.056)	-0.040 (0.614)	315.07 (155.23)	0.065	85.52 (236.61)	0.135	227.38 (204.19)	0.867
Psoriatic Arthritis	**0.197 (0.008)**	**0.173 (0.019)**	**0.136 (0.066)**	**-0.196 (0.009)**	**-0.164 (0.028)**	0.059 (0.468)	526.24 (476.89)	0.700	410.30 (537.79)	0.394	**731.76 (368.08)**	**0.005**
Rheumatoid Arthritis	**0.255 (0.000)**	**0.124 (0.049)**	0.116 (0.068)	**-0.131 (0.040)[a]**	**-0.401 (0.000)**	-0.132 (0.073)	1629.39 (1726.37)	0.788	**522.51 (1879.07)**	**0.000[a]**	1763.58 (1510.80)	0.314
Schizophrenia	-0.035 (0.761)	N/A	0.054 (0.639)	**-0.226 (0.046)**	0.110 (0.340)	**0.424 (0.000)**	1646.23 (1670.99)	0.895	**1155.25 (1725.34)**	**0.049**	1819.52 (1588.47)	0.253
Systemic Sclerosis	-0.005 (0.968)	0.207 (0.066)	0.056 (0.622)	-0.153 (0.176)	**0.284 (0.011)**	-0.206 (0.127)	1077.39 (533.73)	0.165	993.62 (1030.37)	0.901	1131.18 (954.60)	0.466

*NA: not available/applicable a: Hypothesis testing results (H3)

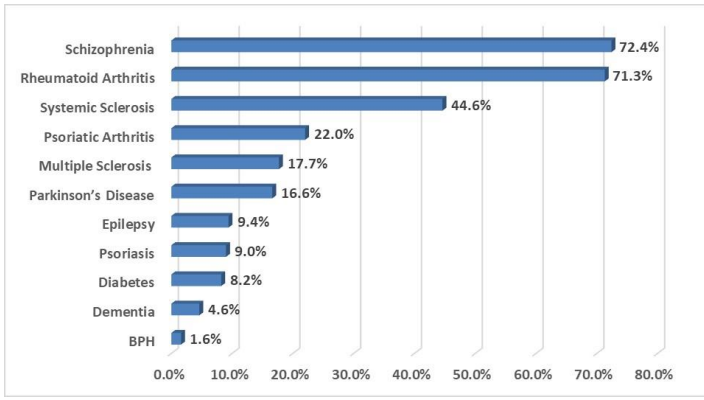

Figure 12. indirect cost as a percent of GDP/capita for eleven NCDs in Hungary.

Our results emphasise that indirect costs can comprise a large portion of the total economic burden of NCDs. Indirect cost as a proportion of total cost measure has proven to be inadequate to facilitate interregional or even intraregional transferability of the results as it often concludes major international discrepancies. On the other hand. The measure of indirect cost proportion out of the national GDP/capita was demonstrated to be beneficial for PL results transferability by minimising costs divergence. Moreover, our results concluded a significant association between health status ($P = 0.040$) and educational level ($P < 0.000$) with PL (accept H3), we presume that incorporating extra adjustment measures over and above the GDP/capita indicator to address local population specificities, such as the human capital index (HCI) and health expenditure (HE), can be beneficial in transferring PL costs between regions. Specifically, given that musculoskeletal diseases have been demonstrated to be one of the most indirect cost-intensive NCDs, we chose to test our transferability hypothesis using musculoskeletal disease PL costs given the disease's significance among other NCDs.

IV.5. REGIONAL ESTIMATES AND TRANSFERABILITY OF PRODUCTIVITY LOSS COSTS OF MUSCULOSKELETAL DISEASE

Table 3. Annual PL costs per patient, means, and standard deviations stratified by country after normalization to reflect 2020-euro value.

Region/Country	PL cost item type	Number of cost items	Mean (SD)
Hungary	Absenteeism	3	62.0 (41.6)
	Long-term disability	1	2652.24 (na)
	Premature retirement	2	4484.7 (2896.2)
	Short-term disability	1	238.65 (na)
	Total Cost	3	4015.4 (2505.1)
Poland	Absenteeism	3	975.8 (188.3)
	Long-term disability	6	1130.1 (659.2)
	Short-term disability	3	198.2 (43.0)
	Total PL Cost	3	3434.1 (1347.8)

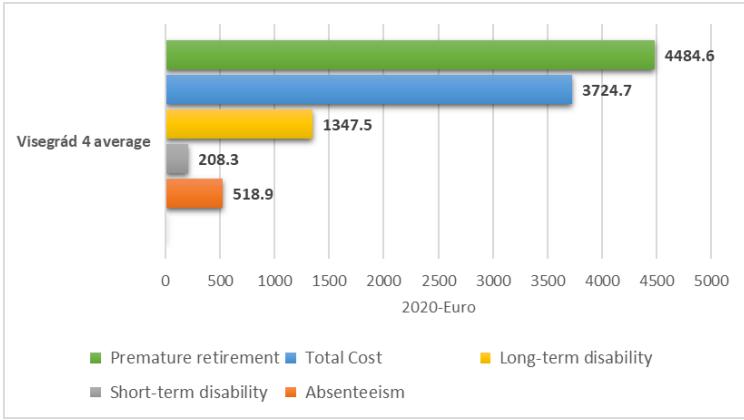

Figure 13. Annual PL cost means per patient for the V4 stratified by PL type.

Table 4. Tunisia's mean PL cost estimates based on the proposed five methods presented in 2020-euro value.

PL cost item type	PL hours back calculation	GDP+HCI	GDP	Wage ratio	GDP+HE
	Method 1 (SD)	Method 2 (SD)	Method 3 (SD)	Method 4 (SD)	Method 5 (SD)
Absenteeism	644.6 (626.8)	74.3 (72.9)	106.5 (105.8)	529.6 (519.3)	114.8 (116.6)
Short-term disability	300.2 (120.0)	30.4 (6.8)	42.7 (8.3)	217.6 (48.6)	44.1 (20)
Long-term disability	1942.0 (1621.9)	197.1 (128.6)	276.4 (170.3)	1406.7 (920.3)	285.7 (160.2)
Premature retirement	5391.0 (2538.3)	701.1 (452.7)	916.8 (592.1)	5019.2 (3241.4)	815.9 (526.9)
Total PL	4907.4 (1744.8)	558.3 (267.4)	763.0 (349.1)	3989.0 (1915.1)	749.6 (325.4)

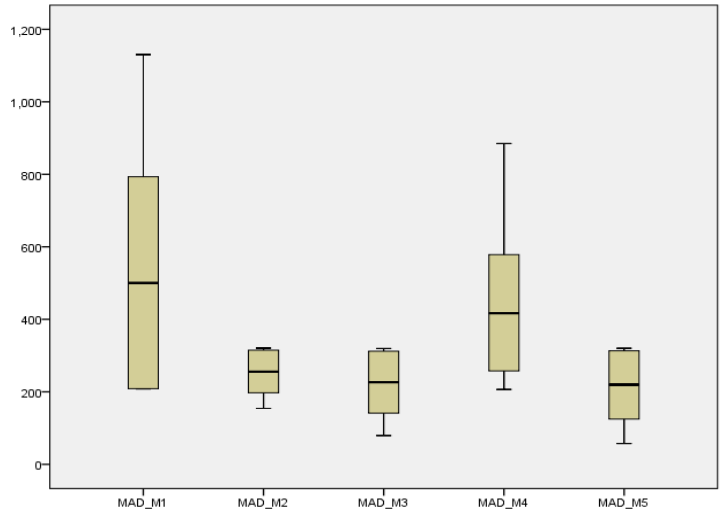

Figure 14. Box plots of absenteeism MADs for each adjustment method. The y-axis represents the cost difference between our methods estimates and Tunisia's reference value.

In this chapter, we provided a V4 regional average for PL costs stratified by type and normalised to reflect 2020-euro value. We also confirmed that country differences in normalised PL cost estimates are probably negligible within the same region accepting our fourth hypothesis (accept H4). Cross-regionally; we demonstrated the superiority of GDP-based adjustments (M2, M3, and M5) compared to wage-based adjustment methods (M1 and M4) in PL costs transferability. We also showed the usefulness of the HCI in contributing to the increased precision of transferred PL cost estimates using the GDP-based method (accept H5). We finally showed that using the health expenditure as an additional adjustment factor results in an insignificant increase in PL estimates accuracy at the expense of lowering precision (reject H6), rendering the method's usefulness limited.

V. CONCLUSIONS AND PRACTICAL IMPLICATIONS

Our work has identified several key findings and practical implications for the MENA, V4, and regional PL costs transferability while our hypotheses results shed light on common domains and helped steer the research direction. We found that HTA is a scarcely addressed topic in the MENA region, and any valid efforts in building the field are of great value. Data and expertise scarcity are key limiting factors in HTA research growth as demonstrated by the low number of publications and authors in the field. On the other hand, and although the CEE is in better shape, yet the local scientific output comprises less than half of the total regional HTA scientific output, suggesting that international collaborations with more advanced health systems are still fairly active in contributing to knowledge transfer into the CEE region. A similar approach of knowledge sharing can be beneficial to seed HTA efforts in the MENA.

Our MENA scoping review of health economic evaluations identified and categorised the comparative research in the region facilitating future inter- and intraregional HTA collaborations based on mutual interest domains. We saw that NCDs underrepresentation among the region's health economic research was significant, which was probably due to the much larger attention to infectious and respiratory diseases, in light of limited local expertise. We also noticed that the journal rank is not necessarily a good indicator of an evaluation's quality, as sub-standardised evaluations may be published in response to the region's research scarcity. Health economists should pay attention to the accuracy and usability of these results. Funding was a major setback in the region as almost half of the evaluations were either non-funded, or no funding statement was mentioned. Periodic, targeted funding and local capacity building are keys to vitalise the region's health economic base.

Productivity loss significance in social welfare was demonstrated in both regions. Mental and musculoskeletal diseases were the highest consumers of patients' productivity restricting as high as 70% of the patient's economic productive capacity as shown in our Hungarian NCD patient population. Education and health-related quality of life were of great significance in predicting PL costs, while hospital admissions showed to be the most cost-intensive utility in NCD management. Policies ensuring early started effective treatments, and targeted budget allocations for high PL NCDs are ought to yield significant socioeconomic returns in the medium and long term.

Our updated V4 regional average for musculoskeletal disease PL costs provides a more complete picture of the societal burden of musculoskeletal disease in the V4 region, as close to none of the identified studies reported all patient-related PL cost types (i.e. mortality, absenteeism, presenteeism, early retirement, short and long term disability). Except for presenteeism, a normalised estimate was reported for each type of PL costs separately to be used as a quick-updated guide for policymakers from the V4 in attaining a more complete picture of the monetary impact of musculoskeletal disease PL within their jurisdictions.

For PL costs transferability, health economists are advised to adopt a balanced pooling approach rather than utilising costs from a single study. Furthermore, disregarding the underlying methodological and theoretical aspects of the studies can lead to misinformed policy decisions. Ensuring that the pooling is done for similar methodological studies is crucial in attaining precise PL estimates. Moreover, and provided the significant global discrepancies in average human capital output, fine tweaking the transferred PL costs as per the projected national human capital output can provide more precise estimates for policymakers in other parts of the world. Adjusting for GDP and HCI combined, can significantly contribute to increasing the precision of transferred PL estimates.

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VII. OWN PUBLICATIONS RELATED TO THIS DISSERTATION

Journal papers

Rashdan, O., & Brodszky, V. (2020). Productivity Loss in Patients With Chronic Diseases: A Pooled Economic Analysis of Hungarian Cost-of-Illness Studies. Value in Health Regional Issues, 22, 75-82.

Zrubka, Z., **Rashdan, O.**, & Gulácsi, L. (2020). Health economic publications from the Middle East and North Africa Region: a scoping review of the volume and methods of research. Global Journal on Quality and Safety in Healthcare, 3(2), 44-54.

Conference papers, abstracts and presentations

Rashdan, O., & Alshafeey, M. (2019). HTA in CEE Countries: A Bibliometric Analysis of Research. In Proceedings of FIKUSZ Symposium for Young Researchers (pp. 192-203). Óbuda University Keleti Károly Faculty of Economics.

Conference abstracts and poster presentations

Rashdan, O. & Brodszky, V. (2019). PP38 Productivity Loss In Patients With Chronic Diseases: A Pooled Analysis. International Journal of Technology Assessment in Health Care, 35(S1), 44-44.

Rashdan, O., Zrubka, Z., & Gulácsi, L. (2020). PMU10 A Scoping Review Of Health Economic Evaluations From The Middle East And North Africa Region. Value in Health, 23, S234-S235.

Rashdan, O., Brodszky, V., Péntek, M., Gulácsi, L., & Zrubka, Z. (2020). PNS32 Towards a Healthcare Cost Catalogue for Middle EAST and North Africa: A Systematic Review of Productivity Loss Costs Reported in Health Economic Publications between 1989-2019. Value in Health, 23, S649