Poster code: EE332

Using Real-World Evidence to Estimate the Societal Burden of Obstructive Hypertrophic cardio myopathy in Norway: Productivity Losses from Absenteeism and Premature Death based on excess mortality

Susanne Gerda Værnø,[1] Francisco Oteiza, [1] Christoffer Bugge, [1] Pilar Martin-Vivaldi, [2] Krister Nyløkken [2]

[1]Oslo Economics, Oslo, Norway; [2]Bristol Myers Squibb, Oslo, Norway

Background

- Obstructive HCM is a chronic, myocardial disease largely caused by dysfunction in the sarcomere that can lead to myocardial changes that increase the risk of sudden cardiac death and heart failure. The disease is one of the leading cause of sudden death among the young, and an important cause of heart failure for patients at all ages (1).
- A recent study from the US found excess healthcare resource costs for obstructive HCM patients in the region of €20,121/year [95% CI $18,762-$21,446], compared to a set of matched controls (2). Another study found that obstructive HCM-related costs increased significantly over a 2-year period after diagnosis, mostly due to inpatient hospitalizations and surgical costs (3). A recent study from France found that sick leave and disability account for 3 percent of the total annual costs for patients with obstructive HCM, equivalent to €332/year for each patient (4).
- It is likely that the disease also poses a significant burden on society in terms of productivity losses, due to both its effect on patient's ability to remain at work, as well as the lost life years stemming from premature death.
- Evidence on these indirect costs of the disease is scarce since cause of death records, the most widely available data source for these estimations, may underestimate the true mortality burden of the disease.
- One study of 4,983 adults of all ages with HCM (both obstructive and non-obstructive) in 7 European countries found excess mortality in the patient population (5), whilst another study found only a slight excess mortality, however increasing with progression of left ventricular outflow tract (LVOT) gradient (6). Another study following 3,675 patients with HCM found that 5 percent died suddenly or had an appropriate implantable cardioverter defibrillator shock over the follow-up period (median 5.7 years) (7).
- The burden of obstructive HCM in Norway in terms of absenteeism and excess mortality is unclear.

Objectives

- Norwegian registry data on the patient population (ages 20 to 90+) is used to advance the understanding of the societal burden of obstructive hypertrophic cardiomyopathy (HCM).
- There is still lacking evidence on obstructive HCM's burden in terms of productivity losses, specifically on how the disease affects patient's capacity to remain at work, and what its mortality burden is.
- To support assessment of new interventions for patients with obstructive HCM, it is necessary to increase the knowledge on what burden the disease places on both patients and society.

Methods

- Health registry data were obtained from the Norwegian Cardiovascular Disease Registry (HKR). Prevalent obstructive HCM patients were identified based on the presence of at least one hospital encounter with an obstructive HCM diagnostic code (ICD-10 I42.1), between 2012 and 2022. Incident patients were defined as all registered patients with 1+ inpatient or outpatient hospital visits for the defined year, and no visits with said diagnostic code during the five preceding years. Incidence is therefore calculated for the 2017 to 2022 period (5-year washout period).
- Data on receivers of health-related benefits was collected from the Norwegian Labour and Welfare Administration (NAV). Data on long-term disability benefits is only available up until 2017, whilst data on temporary sick leave or work assessment allowance is available until 2022. To estimate the number of receivers of disability benefits in 2022, the average patient population growth between 2017 and 2022 was used.
- Productivity losses due to premature death were estimated using an excess mortality approach, comparing age-group-specific all-cause mortality rates of the general Norwegian population with those of the obstructive HCM population using data from the HKR (2017-2022). This method follows previous research conducted on excess mortality of HCM on the European population (5). In an alternative specification, cause of death records for obstructive HCM patients were used instead.
- Employment rates by age group were applied to assign either market or non-market average wages to each patient **(Table 1)**.
- To calculate the production loss from premature deaths the estimated loss per death by age group was multiplied by the number of estimated excess deaths attributable to obstructive HCM.
- All values are discounted at a 4% yearly rate.

Table 1. Norwegian employment rates by age group

	Employment rate
Age group	
15-24	55.1%
25-29	79.3%
30-39	82.0%
40-54	82.1%
55-61	77.2%
62-66	54.9%
67-74	21.3%
75+	0

Source: Statistics Norway

Figure 1. Study design

HCM = Hypertrophic cardiomyapathi. HKR = Norwegian Cardiovascular Disease Registry. NAV = Norwegian Labour and Welfare Administration . CoDR = Norwegian Cause of Death Registry.

Results

Patient population

- 5,403 obstructive HCM patients (aged ≤20) was identified living in Norway as per 31.12.2022 **(Table 2)**.
- There were on average 335 new patients diagnosed with obstructive HCM each year between 2017 and 2022 **(Table 2).**
- 44 percent of the prevalent adult population in 2022 are assumed to be of working age (≤67).

Health-related benefit receivers

- Based on data from NAV on all receivers of health-related benefits in Norway, we find that 36 and 10 patients received work assessment allowance and disability benefits respectively, due to obstructive HCM in 2022.
- In addition, there were a total of 112 obstructive HCM patients receiving short term sick leave benefits during 2022, with an average of 60 days leave per incident. This leads to a total of 7,748 days of sick leave due to obstructive HCM that year.
- Assuming that patients do not receive several types of benefits over the course of one year, approximately 3 percent of the prevalent population received some kind of health-related benefit during 2022.

Table 2. Incidence and prevalence of obstructive HCM in Norway

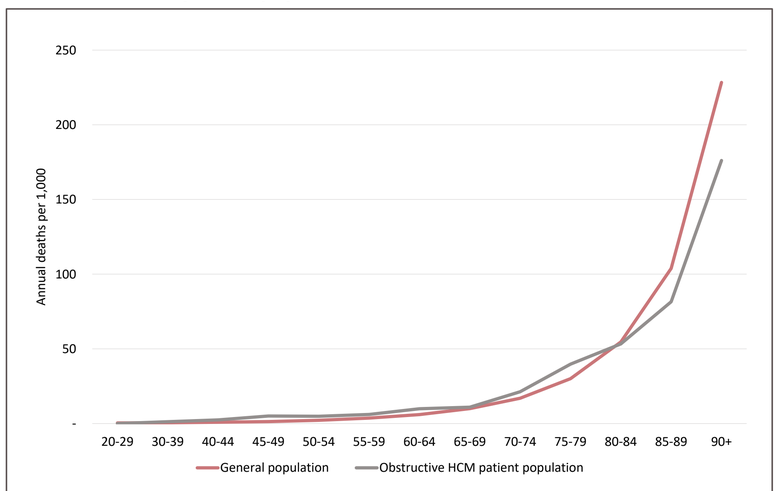
	Average yearly incidence (mean)[a] 2017-2022	Prevalence[b] Per 31.12.2022
Age group		
20-29	4	83
30-39	11	160
40-44	9	148
45-49	15	249
50-54	18	316
55-59	22	415
60-64	33	594
65-69	48	830
70-74	51	804
75-79	57	767
80-84	33	533
85-89	21	334
90+	13	170
All ages		
Total	335	5,403

[a]Incident patients are defined as patients with 1+ inpatient or outpatient hospital visits for the defined year, and no visits with an obstructive HCM diagnosis the five previous years. [b]Prevalent patients are all patients with 1+ in- or outpatient hospital visit between 2017 and 2022, and thus include 2022 incident patients. Source: HKR

Excess mortality

- Excess mortality in the obstructive HCM population (vs general population) was observed in all age groups between 30 and 80. **(Figure 2).**
- Obstructive HCM patients aged ≥80 exhibited lower mortality rates than the average Norwegian population, based on HKR data. The reasons for this lower mortality are not clear and further investigation is needed to give an explanation.
- The difference in (all-cause) mortality rates between obstructive HCM patients and the general population is larger when using mortality data from HKR, than when relying on cause of death registry data, since obstructive HCM is rarely cited as the immediate cause of death.
- There is therefore good reason to believe that cause of death records underestimate the true mortality burden of the disease.

Figure 2. Absolute mortality by age group, general population and obstructive HCM patient population

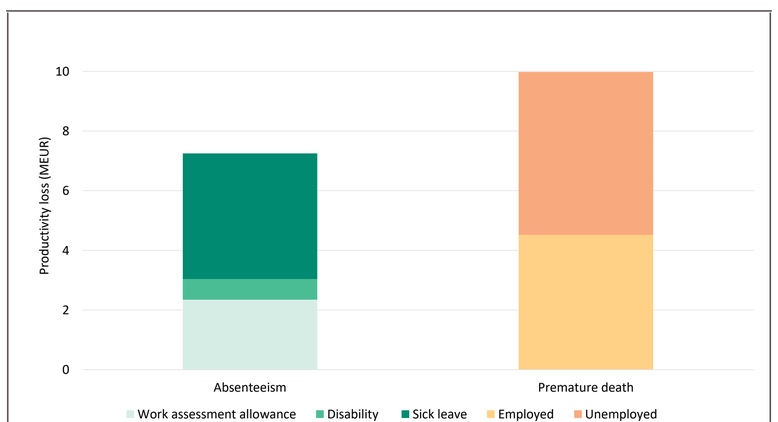


[a]Death of obstructive HCM population show the expected number of deaths among the obstructive HCM patient population. The expected number of deaths is deaths among the obstructive HCM patient population given the death rate of the general population. Source: HKR (Norwegian Cardiovascular Disease Registry) and Statistics Norway.

Productivity losses due to absenteeism

- Productivity loss due to short term sick leave was calculated as the total number of lost days due to obstructive HCM (7,748 days of sick leave) multiplied with the average daily market wage in Norway.
- Productivity losses due to long term sick leave (work assessment allowance) and disability was calculated as the number of patients receiving this pension over the course of one year (assuming that these patients receive the benefit for the full year), calculated by the average yearly salary.
- Based on this methodology, total productivity losses from obstructive HCM in Norway during 2022 were €7 million in terms of absenteeism **(Figure 3)**.
- Short-term sick leave accounted for more than half (58 percent) of the loss from absenteeism. Long-term sick leave (work assessment allowance) accounted for 32 percent while disability pensions accounted for the remaining 10 percent.

Figure 3. Productivity losses from obstructive HCM (in million Euros)

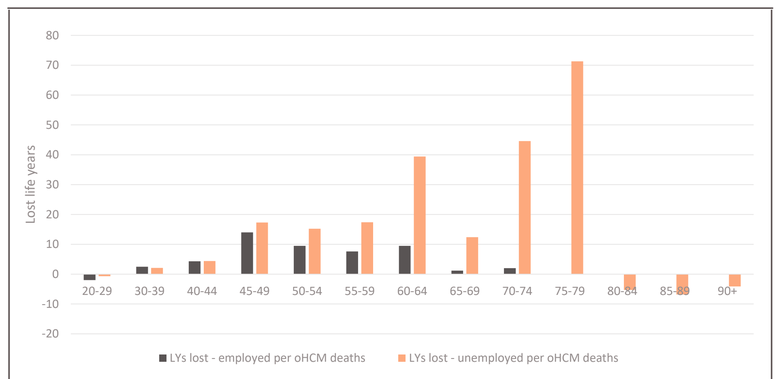


[A] Estimated productivity losses of obstructive HCM 2022, in terms of absenteeism and premature death.

Productivity losses due to premature death

- To estimate the productivity loss due to premature death a value was placed on leisure time with the non-market wage and a market wage was placed on life years lost in employment.
- We find a total productivity loss due to premature death among obstructive HCM patients in 2022 at €10 million, accounting for productivity losses among all obstructive HCM patients, both those employed and unemployed **(Figure 3)**.
- Only including productivity losses from years employed however reduces the loss from €10 M to €4,5M, as the non-market wage is lower than the market wage.
- A patient that dies at a young age will have both a significant loss of employed and unemployed life years. With increasing age of death, the total loss of life years decreases, whilst the relative loss of employed life years will decrease. For those that die after the age of 67, the years lost in employment, is close to zero **(Figure 4)**.
- Of the 200 life years (undiscounted) estimated lost due to obstructive HCM, 50 are years in employment, based on Norwegian employment rates per age group.

Figure 4. Total[a] lost life years attributable to obstructive HCM by age at time of death (annual, undiscounted)



[a]The figure describes the total annual number of lost life years for the prevalent population with obstructive HCM by age group. The calculation is based on the difference in the number of deaths among the obstructive HCM patient population compared to the general population mortality rate within each age group (as shown in Figure 2) and the expected remaining life years for a person within each age group.

Discussion

- The societal burden from obstructive HCM is underestimated if it ignores losses due to premature death and absenteeism.
- The presented estimations suggests that obstructive HCM-related mortality is underestimated for most age groups when using cause of death records from the CoDR.
- Calculating excess mortality with HKR data (preferred method), obstructive HCM patients die at a higher rate than the general population compared to what the CoDR suggests, especially at young ages, which has large impacts on estimated losses.
- Obstructive HCM patients 80 years and above have significantly lower mortality rates than the general population. This could, for example, be due to closer follow-up of these patients by the healthcare sector. It is also possible that the Covid-19 pandemic has had an impact on the mortality rates. Assuming the same mortality rates for these patients as for the general population (i.e. no excess mortality for patients aged ≥80), the total production losses from premature death rise to €14M.
- Few studies have estimated the production losses from premature death. As demonstrated, premature death is a significant source of production losses stemming from obstructive HCM, exceeding the loss from absenteeism by 40 percent.
- Not accounting for these deaths leads to an underestimation of the true burden of obstructive HCM.

Limitations

- All patients with at least one hospital encounter with an obstructive HCM diagnosis (ICD-10 I42.1) registered in the HKR since 2012 was included. There may be a degree of misclassification in hospital records, but this should be small. There may also be a number of patients who have been diagnosed with the disease before 2012 (and never been registered with this diagnostic code since). These patients are thus not included in the dataset and may be the reason for the low mortality estimates among the most advanced age cohorts.
- Data on disability benefits is available only until 2017, so this was extrapolated to 2024 using the observed growth in number of patients. The number of benefits receivers (sick leave, work assessment allowance) is available at the ICPC-2 K84 diagnosis level, while disability benefits data is at the 142.1, I42.2. and I42.5 level. Patients were assigned to the obstructive HCM group based on the observed shares of hospitalization for these broader groups.
- It was assumed that no patients receive several types of benefits over the course of one year, however it is likely that some receive two types of benefits as they progress through the system.
- It is likely that the Covid-19 pandemic has had an impact on number of deaths in the period of 2020-2022, however this effect is unknown and has not been addressed in this analysis.
- Productivity losses due to absenteeism are proxied based on observed health-related benefit receipt. This of course may vary across countries and social welfare systems. The results are thus sensitive to the institutional context in which patients live.

Conclusion

- Obstructive HCM carries a significant mortality burden, particularly among working-age patients. The productivity losses from premature death resulting from this are rarely included in studies of the societal burden of obstructive HCM.
- The excess mortality burden estimated from registry data from the Norwegian Cardiovascular Registry is higher than when using cause of death records for most age groups (except for patients aged 80 and above). Employing death rates from the Norwegian Cause of Death Registry would underestimate the true mortality burden of obstructive HCM on the working age population.
- Productivity losses from obstructive HCM in Norway amount to approximately €7M from absenteeism and €10M from premature death, annually and in present value terms.
- Indirect costs per obstructive HCM patient (absenteeism and premature death) amount to €3,435/year, approximately one sixth of the excess healthcare resource use cost burden estimated for these patients in the literature.

References

1. Cooper RM., et al. *Can J Cardiol*. 2017; 33: 1254-1265.
2. Jain S. S., et al. *J.Med.Econ*. 2021;24:1115-123.
3. Butzner M., et al. *AHJ Plus*. 2022; 13. doi: https://doi.org/10.1016/j.ahjo.2022.100089
4. Charron, P., et al. Poster presentation at ISPOR Europe 2023; November 12-15; Copenhagen; Poster number: EE155
5. Lorenzini M., et al. *JAMA Cardiol*. 2020; 5:73-80.
6. Sorajja P., et al. *J AM Coll Cardiol*. 2009; 54: 234-241.
7. O'Mahony C., et al. *Eur Heart J*. 2014; 7:2010-20.

Acknowledgments

- This study was supported by funding from Bristol Myers Squibb

Disclosures

- Krister Nylokken and Pilar Martin-Vivaldi are employees and shareholders of Bristol-Myers Squibb and may hold stock options. Francisco Oteiza, Christoffer Bugge and Susanne Værnø are employees of Oslo Economics, which received funding from Bristol Myers Squibb for this study.

Presented at ISPOR Europe 2024; November 17-20, 2024; Barcelona, Spain

Email: sgv@osloeconomics.no