Societal Impact Analysis of Introducing Elexacaftor/Tezacaftor/Ivacaftor (ELX/TEZ/IVA) in the Management of People With Cystic Fibrosis in Germany: A Paid and Unpaid Work Productivity Approach

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BACKGROUND

- Cystic fibrosis (CF) is a rare genetic disease caused by mutations in the CF transmembrane conductance regulator (*CFTR*) gene.[1,2] This chronic, progressive disease is characterized by loss of lung function, pulmonary exacerbations, and, historically, lung transplantation or death. These conditions adversely impact the lives of people with CF (pwCF) and their families
- CFTR modulators (CFTRm), small molecules that target the underlying cause of the disease, represent a major advancement in the treatment of CF[3-5]
- Clinical studies of elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA), a triple-combination regimen of CFTRm, have demonstrated unprecedented benefits for pwCF, including improvements in lung function and reductions in pulmonary exacerbations, transplantations, and death.[6-11] The broader societal implications of these improved health outcomes have not been quantified
- The aim of this societal impact analysis was to quantify the impact of ELX/TEZ/IVA among pwCF aged ≥6 years in Germany with at least one *F508del* mutation, using the WifOR Institute approach, with a focus on work productivity-related losses in monetary terms

METHODS

Model Overview

- The societal impact related to work productivity was estimated by monetizing the benefits of reduced morbidity and mortality among pwCF treated with ELX/TEZ/IVA, based on their ability to perform both paid and unpaid work (**Figure 1**)
- An individual patient-level simulation model was developed to derive lifetime health benefits of treatment with ELX/TEZ/IVA and standard of care (SoC) in Germany
- Health benefits for ELX/TEZ/IVA and SoC alone were estimated in terms of years of life lost (YLLs) in paid and unpaid work (YLLs paid/YLLs unpaid) and years lived with disability (YLDs) in paid and unpaid work (YLDs paid/YLDs unpaid). These parameters were used to calculate disability-adjusted life years (DALYs) (**Figure 2**)
- The impact of treatment with ELX/TEZ/IVA was measured by averted DALYs (ADALYs) compared with SoC
- ADALYs were subsequently translated into the monetary value of paid and unpaid activities to estimate the total societal impact of ELX/TEZ/IVA among pwCF aged ≥6 years in Germany with at least one *F508del* mutation
- Productivity measurements of paid work activities were valued using the human capital approach (HCA), whereas unpaid work activities were valued using the proxy good approach
- Additional aspects of socioeconomic value (e.g., community well-being, tax contribution) were not assessed due to data limitations. Direct medical costs were out of scope

### Figure 1. Work Productivity-Related Societal Impact Analysis Model
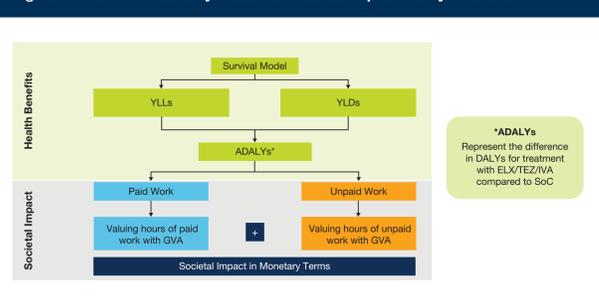
ADALYs, averted disability-adjusted life years; DALYs, disability-adjusted life years; ELX/TEZ/IVA, elexacaftor/tezacaftor/ivacaftor; GVA, gross value added; SoC, standard of care; YLDs, years lived with disability; YLLs, years of life lost.

Health Benefits

- A person-level simulation model was developed to estimate the lifetime clinical benefits of ELX/TEZ/IVA compared with SoC among pwCF aged ≥6 years with at least one *F508del* mutation in Germany. The technical details and clinical inputs of the model have been described previously[12]
- DALYs were calculated by combining mortality (YLLs) and morbidity (YLDs), based on the age of retirement for paid work and normal life expectancy for unpaid work
  - YLLs in unpaid work measure the impact of premature mortality caused by CF, calculated by subtracting the age at death of an individual with CF from the expected age of death in the general population
  - YLLs in paid work quantify the impact of the disease on the number of years an individual would have continued to engage in paid work had they not died prematurely from CF
  - YLDs in unpaid and paid work represent the number of years lived with a reduced quality of life due to CF, reflecting the years of healthy life lost due to disability. As with YLLs, YLDs in paid work were calculated based on the age of retirement, while YLDs in unpaid work were calculated based on the average life expectancy in Germany
- **Figure 2** summarizes the model inputs used to estimate the health benefit of ELX/TEZ/IVA and SoC

Figure 2. Model Inputs Used to Derive Health Benefits for Paid and Unpaid Work
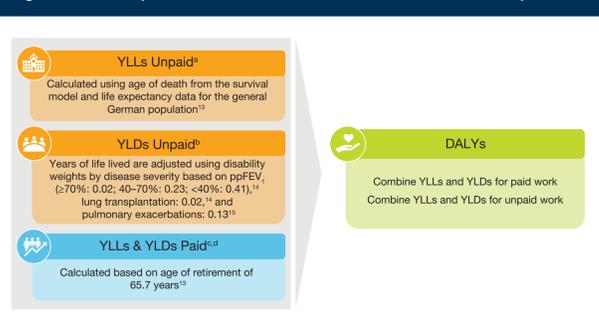
[a]YLLs for unpaid work = standard remaining life expectancy at age of death-age at death caused by CF. [b]YLDs for unpaid work = time spent in health state×disability weight in health states. [c]YLLs for paid work = age of retirement-age at death caused by CF. [d]YLDs for paid work = time spent in health state×disability weight in health states up until retirement age.

Quantifying Paid Work

- The HCA and gross value added (GVA) were used to quantify and monetize paid productivity losses among pwCF due to CF
  - The HCA estimates productivity losses incurred during an individual's working life by monetizing the lost output or earnings with a relevant value of production, such as individual or average wages[16,17]
  - GVA measures the production value of goods and services minus the value of intermediate goods and services[18]
- **Figure 3** describes each step used to quantify productivity loss from paid work among pwCF treated with ELX/TEZ/IVA compared with SoC alone

Figure 3. Flow Diagram of the Steps to Estimate Productivity Loss for Paid Work

CF, cystic fibrosis; DALYs, disability-adjusted life years; GVA, gross value added; UK, United Kingdom; YLDs, years lived with disability; YLLs, years of life lost.

Table 1. Daily Paid Working Hours per Age and Gender in Germany[20]

Age (Years)	Hours per Day (Male)	Hours per Day (Female)
15–25	6.69	6.11
30–49	8.02	6.09
≥50	7.65	5.83

Quantifying Unpaid Work

- The proxy good approach was used to quantify time spent on unpaid labor
  - Reid's "third person criterion" was used to identify activities that should be categorized as unpaid work. According to this principle, activities are classified as unpaid work, rather than leisure activities, if it could be performed by a third person[22]
- **Figure 4** outlines the steps to quantify productivity loss associated with unpaid work among pwCF treated with ELX/TEZ/IVA compared with SoC

Figure 4. Flow Diagram of the Steps to Estimate Productivity Loss for Unpaid Work
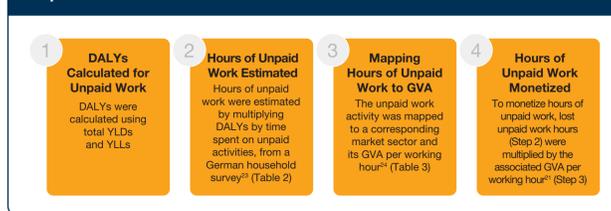
CF, cystic fibrosis; DALYs, disability-adjusted life years; GVA, gross value added; YLDs, years lived with disability; YLLs, years of life lost.

Table 2. Daily Unpaid Working Hours in Germany by Activity[23]

[a]From left to right: ✔ Activity 1, Constructions and repairs; ☐ Activity 2, Shopping and services; 👪 Activity 3, Household management and help family member; 👕 Activity 4, Laundry, ironing, handicraft, and producing textiles and other care for textiles; 🐕 Activity 5, Gardening; other pet care, tending domestic animals, caring for pets, walking the dog; 🛒 Activity 6, Childcare, teaching, reading, and talking with child; 🍽 Activity 7, Food management and dish washing; 🧹 Activity 8, Cleaning dwelling and household upkeep; 🎭 Activity 9, Voluntary work.

Table 3. GVA per Working Hour for Unpaid Work Activities in Germany

Unpaid Work Activity	Corresponding Market Sector[24]	GVA per Working Hour[a] (€)
Laundry and textile care	Administrative and support service activities	41
Gardening and pet care	Agriculture, forestry and fishing	33
Childcare	Education	45
Food management and dish washing	Accommodation and food service activities	18
Cleaning dwelling and household upkeep	Administrative and support service activities	41
Construction and repairs	Construction	22
Shopping, household management, and voluntary work	Administrative and support service activities	41

GVA, gross value added. [a]GVA per working hour is calculated by dividing hours worked by total GVA for each sector.[11]

RESULTS

Health Benefits

- Treatment with ELX/TEZ/IVA resulted in substantial health benefits, including improved survival and reduced disability due to CF
- In the simulated cohort, the mean baseline age was 23.3 years, and the mean baseline percent predicted forced expiratory volume in 1 second (ppFEV$_1$) was 67.1 percentage points
- PwCF treated with ELX/TEZ/IVA were projected to live to 70.9 years, an additional 31.8 years of life compared with SoC (predicted median survival for SoC: 39.1 years)
- Treatment with ELX/TEZ/IVA was projected to have a reduction in YLLs and YLDs for both paid and unpaid work when compared with SoC (**Figure 5**)
  - For paid work, the simulation projected a 68% reduction in the YLLs and 31% reduction in the YLDs among pwCF treated with ELX/TEZ/IVA when compared with SoC
  - For unpaid work, the simulation projected a 52% reduction in the YLLs and 8% reduction in the YLDs among pwCF treated with ELX/TEZ/IVA when compared with SoC

Figure 5. Projected Lifetime Health Benefits of ELX/TEZ/IVA Treatment in pwCF Aged ≥6 Years in Germany
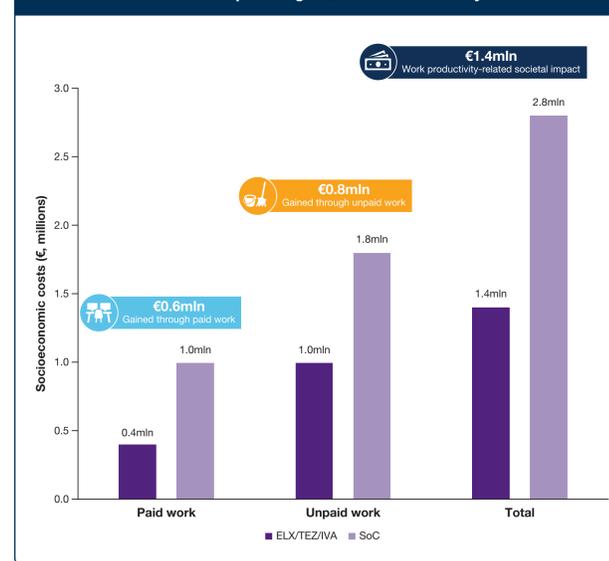

DALYs, disability-adjusted life years; ELX/TEZ/IVA, elexacaftor/tezacaftor/ivacaftor; pwCF, people with cystic fibrosis; SoC, standard of care; YLDs, years lived with disability; YLLs, years of life lost.

Work Productivity-Related Societal Impact of ELX/TEZ/IVA

- The simulation projected that pwCF treated with SoC endured a lifetime productivity loss of €2.8 million (mln) (**Figure 6**)
  - Of this total, €1.8mln was attributed to unpaid work, and €1mln to paid work
- PwCF treated with ELX/TEZ/IVA were projected to have a 50% reduction in productivity loss when compared with SoC, resulting in a mean per person with CF improvement of €1.4mln in lifetime productivity (**Figure 6**)
  - This improvement included €1.0mln attributed to unpaid work (40% reduction vs SoC) and €0.4mln attributed to paid work (60% reduction vs SoC)

Figure 6. Projected per Person Work Productivity-Related Societal Impact of ELX/TEZ/IVA Treatment in pwCF Aged ≥6 Years in Germany

ELX/TEZ/IVA, elexacaftor/tezacaftor/ivacaftor; mln, million; pwCF, people with cystic fibrosis; SoC, standard of care.

Limitations

- This analysis covers only a specific portion of the potential societal impact of ELX/TEZ/IVA; other aspects of societal impact were not included in this analysis
- Obtaining direct CF-related data was not always feasible; therefore, proxy disease data were used for disability weights
- UK-specific inputs were used in the survival model where country-specific data for Germany were unavailable

CONCLUSIONS

- The simulation projects a substantial societal burden among pwCF treated with SoC due to increased mortality and morbidity
- This analysis provides a perspective on socioeconomic value generated by ELX/TEZ/IVA in Germany, highlighting the positive impact of its clinical benefits and extended survival on work productivity
- Further research is recommended to estimate additional aspects of the societal impact of ELX/TEZ/IVA and next generation CFTRm

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