Assessment of the economic impact of aids at national and multi-national level : development of a scenario-analytic approach to support health-care policy

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**ASSESSMENT OF THE ECONOMIC IMPACT OF AIDS
AT NATIONAL AND MULTI-NATIONAL LEVEL;**

**development of a scenario-analytic approach
to support health-care policy**

**ASSESSMENT OF THE ECONOMIC IMPACT OF AIDS
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**development of a scenario-analytic approach
to support health-care policy**

**DE ECONOMISCHE CONSEQUENTIES VAN AIDS
OP NATIONAAL EN MULTINATIONAAL NIVEAU**

scenario analyse ter ondersteuning van gezondheidszorgbeleid

(met Nederlandstalige samenvatting)

PROEFSCHRIFT

ter verkrijging van de graad van doctor
aan de Universiteit Maastricht,
op gezag van de Rector Magnificus, Prof Dr AC Nieuwenhuijzen Kruseman
volgens het besluit van het College van Dekanen,
in het openbaar te verdedigen
op vrijdag 9 oktober 1998 om 14.00 uur

door

Maarten Jacobus Postma

geboren op 29 januari 1960, te Groningen

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Aan mijn moeder
Ter nagedachtenis aan mijn vader
Voor Geert

Curriculum vitae

Maarten Jacobus Postma was born on 29 01 60 in Groningen (the Netherlands). After high-school finals in 1978 (Heymans College Groningen) he entered University. The university career (Groningen University) comprised one year of Historical Sciences and 6 years of Econometrical and Actuarial Sciences. On-the-job training was performed at the Medical Center Leeuwarden, during which period he developed a simulation-model to assess the optimal distribution of hospital capacity over the medical specialisms.

During 1986-1988 he worked as a business econometrician in the marketing department of FBTO insurance company. Responsibilities concerned quantitative analyses of strategic decisions and development of Management Information Systems. His next job was at the National Institute of Public Health and the Environment (RIVM) as a researcher in health economics.

The basis for this thesis was provided by several research activities at RIVM, such as EU-projects on AIDS economics and a consultancy for the Dutch Association of Life Insurers. One of his current research projects concerns the development of guidelines for cost-effectiveness analysis in infectious diseases through linking epidemiological modelling and costing information (applications for AIDS, Influenza, Chlamydia, Hepatitis and Meningitis).

He currently gives courses and lectures in cost-effectiveness analysis in infectious diseases. Furthermore, he works with students (economical, medical and pharmacological) to develop their skills in cost- and cost-effectiveness analysis.

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Key Messages

Estimates of the resources and costs of hospital care for HIV/AIDS can be used for planning at the national or multi-national level if a standardized approach in epidemiological modelling, economic data-gathering and severity-staging of disease is applied.

Lifetime costs from the time of HIV-infection onwards are estimated to amount 76 000 ECUs in the Netherlands, hospital costs constitute almost 90% of this figure.

In the Netherlands, approximately one quarter to a half percent of total hospital costs will be required for HIV/AIDS by the end of the century, a sizeable but manageable proportion.

Hospital bed needs for AIDS in the EU by the end of the century will amount 0.5% to 0.65% of all hospital beds available in the EU.

Application of the dynamic cost-of-illness approach developed in this thesis is a prerequisite for many economic evaluations in infectious diseases.

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Ik draag dit proefschrift op aan mijn moeder. De steun die ik altijd van haar gekregen heb is nu tevens uitgebreid naar de volgende generatie. Haar grote betrokkenheid bij de opvoeding van haar kleinkinderen is een grote verrijking van hun leven en gaf mij vaak de gelegenheid woensdagmiddagen en zondagen aan het proefschrift te werken.

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Summary

During the second half of the 1980s interest arose for the economic consequences of the Human Immunodeficiency Virus (HIV) that causes AIDS (Acquired Immunodeficiency Syndrome). In European Union (EU) member states, relevant impacts of AIDS on in particular health-care costs and life-insurance losses. This thesis elaborates these issues, the first step for which had been taken in the beginning of the 1990s. Some of the methods used in the cost-of-illness approach were adopted. However, this approach had to be extended to include emerging treatment and care patterns of a new disease, for questions of care capacities - especially hospital beds - and the specification with respect to the development over time of a significantly spreading infectious disease, therefore requiring a link with epidemiological modelling. In short, the method used here can be labelled "dynamic cost-of-illness" approach. Methodologically, this can be considered an extension of existing methods of economic evaluation in health care. (Chapters 1-2)

To help public-health HIV/AIDS planning of health-care facilities in the EU, preliminary economic impact scenarios were developed already in 1993. Using a simulation model, routine AIDS surveillance-data, information on disease progression and hospital-based studies on the health-care utilization were integrated in scenarios at an aggregated EU-level. Evaluation of published studies on hospital resource utilization and costs for HIV/AIDS patients showed that significant differences exist between countries and studies. These differences are partly related to methodology, illustrating the need for a standardized costing approach. Standardized health-care information in different EU-countries is a prerequisite for construction of multi-national scenarios. (Chapters 3-4)

A specification of the approach to the Netherlands showed that forecasted hospital bed needs for HIV/AIDS by the end of the century is limited compared to projections for coronary heart disease and stroke, but approaches those for lungcancer, pneumonia and diabetes. Hospital costs were estimated to be 85% of total health-care costs for HIV/AIDS in 1993. Scenarios indicated a decreasing share of outpatient costs, illustrating the growing relative importance of the care-intensive stages of HIV disease. (Chapter 5)

To cope with emerging Dutch questions in life insurance a consultancy project was conducted. In particular, losses were feared if groups of persons living with HIV and AIDS (PLWHAs) were accepted for insurance, and possibilities to compensate insurers

Summary

were discussed. For this purpose, the scenario approach was extended with age-specific analyses and assumptions on income position and life-insurance needs of PLWHA. Possible demand of PLWHAs was estimated for pension, mortgage and temporary-risk insurance in several scenarios. The size of the Life-insurance Fund, that should provide compensations for insurer's losses, is estimated at f50 to 125 million. (Chapter 6)

Progression of AIDS disease is staged in two substages: the final half year of AIDS preceding death (*late* stage) and the foregoing period (*early/chronic* stage). The Dutch hospital costs per person-year in the late stage are almost three times those in the chronic stage. More than half of lifetime hospitalization costs are generated in the late stage. It is illustrated that the choice of an appropriate disease-staging is crucial and averts structural biases in projections of health-care needs. Criteria are formulated for the minimal quality of databases on utilization and costs of health care for PLWHAs. (Chapter 7)

Using the defined quality-criteria, six national studies on the utilization of hospital care for AIDS are selected to provide the data for EU-scenarios. Epidemiological parts of the scenario's are based on standardized modelling for the backcalculation from registered AIDS cases to HIV incidence in the past and the projection of future AIDS incidence, prevalence and mortality. Next, estimated health-care resource needs are linked to epidemiological outcomes. Several scenarios render different possible future health-care resource needs. By the end of the century hospital bed needs of 10 000-12 700 in the EU are indicated, representing 0.5 % to 0.65 % of all hospital beds in the EU. (Chapter 8-9)

Estimates of resources and costs of hospital care for HIV/AIDS can be used for planning at the national or multi-national level if a standardized approach in epidemiological modelling, economic data-gathering and severity-staging of disease is applied. Estimated lifetime costs from the time of HIV-infection onwards are estimated to amount 76 000 ECUs in the Netherlands. In the Netherlands, one quarter to a half percent of total hospital costs will be required for HIV/AIDS by the end of the century. Application of the dynamic cost-of-illness approach developed in this thesis is a prerequisite for many (pharmaco-)economic evaluations in infectious diseases. (Chapter 10)

In this thesis a dynamic cost-of-illness approach is developed for HIV/AIDS. Further research is directed at the development of dynamic cost-effectiveness analysis in treatment and prevention of HIV and other infectious diseases. This research is already in progress.

Samenvatting

Gedurende de tweede helft van de tachtiger jaren onstond er sterke interesse voor de economische "impact" van het Human Immunodeficiency Virus (HIV), dat het Acquired Immunodeficiency Syndrome (AIDS) veroorzaakt. In de Europese Unie (EU) werden aanzienlijke consequenties gevreesd voor met name de gezondheidszorg en de (levens)verzekeringen. Dit proefschrift gaat in op deze kwesties, voortbouwend op onderzoek dat reeds aan het begin van de negentiger jaren startte. De methodiek sluit aan bij de "Cost-of-illness" benadering. Deze benadering is vervolgens aangepast aan de specifieke omstandigheden van de nieuwe ziekte, waarin veel en snel opeenvolgende veranderingen in behandeling en zorg plaatsvinden. Daarnaast moest rekening gehouden worden met de dynamiek van de HIV-infectie, hetgeen een directe connectie met de modellering van de verspreiding van infectieziekten vereist. De hier gebruikte methode kan als dynamische Cost-of-illness benadering worden omschreven. Methodologisch gezien is deze benadering een uitbreiding van bestaande methoden van economische evaluatie in de gezondheidszorg. (Hoofdstukken 1-2)

Om tegemoet te komen aan de informatiebehoefte voor de planning van gezondheidszorgvoorzieningen werden in 1993 voorlopige economische "impact" scenario's voor de EU ontwikkeld. Binnen een simulatiemodel werden gegevens over de incidentie van AIDS, de progressie-van-ziekte en het gebruik van gezondheidszorg geïntegreerd tot diverse toekomstscenario's. Evaluatie van de studies over het gebruik van gezondheidszorgvoorzieningen en de daaraan verbonden kosten van HIV/AIDS toonden aan dat er aanzienlijke verschillen zijn tussen studies en landen, ook na correctie voor diverse invloeden. Deze verschillen konden gedeeltelijk worden teruggevoerd op methodologische aspecten, hetgeen de noodzaak voor een gestandaardiseerde aanpak van studies naar het gebruik en de kosten van gezondheidszorg bij HIV/AIDS illustreert. Gestandaardiseerde informatie over de gezondheidszorg is een noodzakelijke voorwaarde voor multinationale scenario's betreffende de economische impact van HIV/AIDS. (Hoofdstuk 3-4)

Nadere specificatie voor Nederland toonde aan dat het voorspelde gebruik van ziekenhuisbedden voor HIV/AIDS aan het einde van de twintigste eeuw aanzienlijk lager is dan soortgelijke extrapolaties voor hart- en vaatziekten, echter in de orde van grootte komt van bedbehoefte voor longkanker, longontsteking en diabetes. De ziekenhuiskosten

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werden geschat op 85 % van de totale gezondheidszorgkosten voor HIV/AIDS in 1993. Verschillende scenario's geven een dalend aandeel van de poliklinische kosten te zien. Dit illustreert het toenemende relatieve belang van de HIV-stadia waarin veel klinische zorg nodig is. (Hoofdstuk 5)

In 1995 speelde in Nederland de vraag of er een speciaal fonds (Garantiefonds) zou moeten komen om bepaalde vormen van levensverzekering ook voor HIV-geïnfekteerden mogelijk te maken. Het Garantiefonds zou aangewend moeten worden om levensverzekeraars te compenseren voor uitkeringen aan HIV-geïnfekteerden. Tijdens een consultancy opdracht is de vraag naar pensioen-, hypotheek- en tijdelijk-risico verzekeringen geschat voor groepen HIV-geïnfekteerden. Hiervoor werd de scenario-methodologie uitgebreid met een leeftijdsspecifieke aanpak en veronderstellingen over de inkomenspositie en de behoefte aan levensverzekeringen van HIV-geïnfekteerden. De geschatte omvang van het Garantiefonds bedraagt f50 tot 125 miljoen. (Hoofdstuk 6)

Bij de progressie-van-ziekte voor AIDS zijn twee substadia onderscheiden: het laatste half jaar van AIDS, voorafgaand aan overlijden (*late* stadium) en de daaraan voorafgaande periode (*vroege/chronische* stadium). In Nederland zijn de ziekenhuiskosten per persoonjaar in het late stadium circa drie maal zo hoog als in het chronische stadium. Meer dan de helft van de "lifetime" kosten worden veroorzaakt tijdens het late stadium. Aangetoond wordt dat de keuze voor een adequate indeling van de ziekte in stadia cruciaal is en een structurele overschatting van de gezondheidszorgkosten voor AIDS voorkomt. Tevens worden criteria geformuleerd voor de minimaal vereiste kwaliteit van een observationele studie over het gebruik en de kosten van gezondheidszorg voor HIV/AIDS patiënten. (Hoofdstuk 7)

Aan de hand van de criteria voor minimale kwaliteit zijn zes nationale Europese studies over het gebruik en de kosten van gezondheidszorg voor HIV/AIDS patiënten geselecteerd. Op basis van deze studies zijn scenario's voor de EU ontwikkeld. De epidemiologische achtergrond van de scenario's is gebaseerd op gestandaardiseerde modellering van het "terugrekenen" van gemelde AIDS-gevallen naar de incidentie van HIV in het verleden en het voorspellen van toekomstige AIDS incidentie, prevalentie en mortaliteit. In de volgende stap worden schattingen voor de behoefte van gezondheidszorg gekoppeld met de epidemiologische uitkomsten. Verschillende scenario's tonen diverse mogelijke toekomstige ontwikkelingen voor de epidemiologie en de behoefte aan

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gezondheidszorg. De behoefte aan ziekenhuisbedden in de EU wordt voor het einde van de twintigste eeuw geschat op 10 000 - 12 700, heigeen overeen komt met 0.5% tot 0.65% van alle ziekenhuisbedden in de EU. (Hoofdstuk 8-9)

Schattingen van de middelen en kosten voor HIV/AIDS ziekenhuiszorg kunnen worden gebruikt voor planning op nationaal en multinational niveau indien een gestandaardiseerde aanpak wordt gevolgd voor de epidemiologische modellering, de economische data-vergaring en de indeling van de ernst-stadia van HIV/AIDS. De geschatte "lifetime" kosten vanaf het moment van HIV-infectie bedragen 76 000 ECUs in Nederland. Aan het einde van de twintigste eeuw is een kwart tot een half procent van alle ziekenhuisbedden in Nederland nodig voor de verpleging van patiënten met HIV/AIDS. Toepassing van de dynamische Cost-of-illness benadering uit dit proefschrift is een noodzakelijke voorwaarde voor de uitvoering van (farmaco-)economische evaluatie bij infectieziekten. (Hoofdstuk 10)

In dit proefschrift is een dynamische Cost-of-illness benadering voor HIV/AIDS ontwikkeld. Huidige vervolgwerkzaamheden richten zich op dynamische kosten-effectiviteitsanalyse van preventie en behandeling bij HIV en andere infectieziekten.

List of Abbreviations

AIDS	Acquired Immunodeficiency Syndrome
AZT	Azidothymidine
CDC	Centers for Disease Control
EC	European Communities
EU	European Union
GHI	Chief Medical Inspector (Geneeskundige Hoofdinspectie)
GP	General practitioner
HAART	Highly Active Antiretroviral Therapy
HIV	Human Immunodeficiency Virus
PCP	<i>Pneumocystis carinii</i> Pneumonia
PWA	Person with AIDS
PLWHA	Person living with HIV/AIDS
PYLL	Potential years of life lost
RIVM	National Institute of Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu)
STG	Steering Committee on Future Health Scenarios (Stuurgroep Toekomstscenarios Gezondheidszorg)
UK	United Kingdom
US	United States
WHO	World Health Organization

Chapter 1

General Introduction

This chapter is partly based on book contributions:

JC Jager, MJ Postma, FMLG van den Boom *et al.*: **Epidemiological Models and Socio-economic Information; methodological aspects of AIDS/HIV scenario analysis.** *In*: D Schwefel, R Leidl, J Rovira, MF Drummond (Eds) *Economic Aspects of AIDS and HIV Infection*. Berlin: Springer-Verlag 1989, pp 262-81.

MJ Postma, GJP van Griensven: **AIDS (hoofdstuk 14).** *In*: CW Aakster, G Kuiper, JW Groothoff (Eds) *Medische Sociologie*. Groningen: Wolters-Noordhof 1991, pp 129-36.

JC Jager, MJ Postma, K Tolley, J Kenelly: **Assessment of the Socio-economic Impact of AIDS; from national towards multi-national scenarios.** *In*: D Fitzsimons, V Hardy, K Tolley (Eds) *The Economic and Social Impact of AIDS in Europe*. London: Cassell 1995, pp 40-53.

1.1 Main Initial Questions and Methodological Challenges

During the second half of the 1980s concern came up about the consequences of the Acquired Immunodeficiency Syndrome (AIDS) for health-care systems in European Union (EU) member states [1]. Furthermore, significant effects of AIDS on the economy were feared, such as productivity losses, life-insurance losses and public-sector compensations [2]. It was felt that health-care cost implications and capacity needs would become main issues concerning the general impact of the new disease. This thesis elaborates these research issues, the first step for which had been taken in the beginning of the 1990s. Some of the methods used in the cost-of-illness approach were adopted [3]. However, this approach had to be extended to include emerging treatment and care patterns of a new disease, for questions of care capacities - especially hospital beds - and the specification with respect to the development over time of a significantly spreading infectious disease, therefore requiring a link with epidemiological modelling. In short, the method used here can be defined as the "dynamic cost-of-illness" approach. Methodologically, this can be considered an extension of the existing methods of economic evaluation.

This thesis seeks to provide research contributions to several areas. Firstly, it concentrates on sound methods for measurement of health-care resources and costs and comparisons of results of different studies in this field. Secondly, methods for the assessment and projection of the burden-of-disease and budget impact are developed, and comparisons are made with other diseases and among countries. In detail, the role of the case-mix over severity stages of HIV/AIDS is clarified. Thirdly, the special requirements for linking epidemiological models of infectious diseases and health care information are addressed. The information provided in this thesis can contribute to economic evaluation studies, such as cost-benefit and cost-effectiveness analysis. In fact, knowledge about cost measurement methods, epidemiological developments, burden-of-disease and budget impact is a precondition for any economic evaluation. In terms of methodology the developments in this thesis include infectious disease modelling, multi-model, multi-parameter and multi-national standardized scenario analysis and the linkage of epidemiological modelling and health-care data.

Ultimately, the type of research presented here aims at underpinning health-care policies. As such, research results should provide a sound basis for estimating and forecasting health-care capacity needs and cost impacts. Outside the health-care sector results could benefit tackling questions arising in prevention, life insurances and market-developments for pharmaceutical industries.

1.2 The Epidemic of HIV/AIDS

AIDS is an infectious disease caused by the Human Immunodeficiency Virus (HIV), a retrovirus that can be transmitted through sexual contact, blood and blood products and from mother to child [4-6]. According to the AIDS surveillance case-definition, AIDS is a collective noun for a broad range of illnesses that result from a lowered immune system due to the debilitating effect of HIV [7,8]. Infection with HIV causes a high susceptibility for several rather uncommon infections, particular cancers and psychiatric disorders such as dementia and depression. AIDS is the last stage of HIV infection and up to now AIDS is perceived to be an incurable disease. There is no vaccine for HIV, nor an effectively curative therapy available. There are however some drugs on the market that slow down the progression from asymptomatic HIV infection to AIDS and that prolong survival in the AIDS stage, such as azidothymidine (AZT)/zidovudine, prophylaxis for pneumonia and combination triple therapy [9-11]. Of the recently introduced combination triple therapy the effects on disease progression are promising but as yet uncertain. Prior to the introduction of triple therapy, estimates of the length of the incubation period indicate an average duration of 11-12 years from the time of infection to the first appearance of AIDS symptoms [12,13]. In the incubation period three subperiods can be distinguished. Relatively short subperiods of acute infection and symptomatic pre-AIDS surround an intermediate asymptomatic subperiod of 9-10 years. The average survival time for AIDS patients is estimated at 2-3 years [14,15]. Next to the AIDS surveillance case definition a staging system for HIV has been developed by the Centers for Disease Control (Atlanta; CDC) that is based on the clinical experience of managing HIV infection in patients (CDC stages) [16,17]. The CDC-stages reflect a hierarchical system from acute infection, through asymptomatic seropositivity to clinical symptoms. The final CDC stage (CDC IV) crudely corresponds with AIDS, though small differences in definitions exist.

In the eighties AIDS surveillance systems have been set up [18]. For example, in the US the CDC took up this task. The long incubation period of HIV/AIDS means that AIDS surveillance can only reflect "the top of the iceberg". AIDS cases reported to the surveillance systems provide a minimum estimate of total HIV seroprevalence. National surveillance systems for HIV have proven not to be feasible (*see for example* [19] for the Netherlands). Therefore, several methods have been applied for estimating HIV seroprevalence [20]. In the US, AIDS was first reported at the beginning of the eighties in the cities of Los Angeles, New York and San Francisco [21,22]. HIV was probably first present in the Netherlands in the late-seventies or early-eighties, as the first AIDS

patient was diagnosed in April 1982 [23]. The surveillance of AIDS in the Netherlands is undertaken by the Chief Medical Officer of the State Supervision of Public Health (Geneeskundige Hoofinspectie; GHI) in Rijswijk [24]. Up to December 1996 at least 4288 cases of AIDS had been diagnosed [25]. The estimated number of AIDS diagnoses worldwide amounted to 7.7 million by mid-1996, with the majority (77%) of these cases in African countries [26]. UNAIDS estimated by mid-1996 the worldwide number of persons living with HIV/AIDS at 22 million - with 64% in Africa [27] -, which was slightly higher than the corresponding estimate in *AIDS in the World* [28]. In mid-1996, in the US over half a million of AIDS cases had been reported to the CDC, and an estimated 200 000 European AIDS cases had been diagnosed [26]. In western Europe 640 000 persons were estimated to be living with HIV/AIDS by mid-1996. For the European region the Centre for the Epidemiological Monitoring of AIDS (Paris) provides standardized information on AIDS surveillance and estimations of HIV infections [29]. Recent estimations for the EU, Austria and Switzerland show that during the period 1990-1994 almost 90 000 AIDS cases have been diagnosed, half of which are intravenous drugusers (homosexual men account for 40%) [30].

1.3 Costing and HIV/AIDS; a global view

HIV/AIDS has had and will have a considerable impact on the health-care systems of many countries. As mentioned, the perspective adopted in this thesis is a dynamic cost-of-illness assessment, conducted at the population level. Adjacent areas in health-economics science involve cost-of-illness analysis at the patient level and economic evaluation [31]. Among others, this thesis builds on work described in another thesis on the patient-based registration of HIV/AIDS that has been used in some Dutch hospitals [32]. As an appropriate costing of disease provides a basis for economic evaluation studies, this thesis can contribute to the set-up of such studies in the field of HIV/AIDS and infectious diseases in general.

In a cost-of-illness analysis, several classifications are used for expressing the consequences of disease on resource utilization and costs: direct versus indirect costs, patient-related vs. general program costs and health care vs. non-health care costs [33-35]. These classifications have also been used to express the financial/economic consequences of AIDS [2,36-39]. *Direct* costs arise from the treatment and care of patients in different health-care settings and from research, public information, prevention

and media campaigns. These costs can be linked directly to a specific disease. *Indirect* costs relate to production losses as a result of premature death (potential years of life lost; PYLL) or illness (sickness absence). *Patient-related* costs are those incurred by each individual in a certain disease stage [40]. These costs comprise the direct costs of treatment and care and indirect costs. *General program* costs cover the costs of research, prevention, public information and the maintenance of services for the benefit of the entire population. In this thesis the main focus is the assessment of the patient-related direct costs of HIV/AIDS in the hospital sector. By illustration, some attention has been given to indirect costs based on PYLL, and out-of-hospital costs, such as medication and district nursing costs.

In 1986 the first papers on the health-care costs of persons with AIDS (PWAs) in the US appeared in the literature, most of them focussing on hospital care [41-45]. The first paper in this set [41] is now generally considered to have overestimated lifetime costs per PWA at US\$147 000. The other US-studies gave lower estimates. Expressed per person per year the early US-studies reported cost figures of up to US\$75 000 [44] and 100 000 [41]. Using the data of [42] and predictions of future AIDS incidence produced in 1986, it was estimated that towards the end of the 1980s hospital bed needs for AIDS would approach 1% of all hospital beds available in the US [46]. This type of projection reflected, with pessimistic epidemiological forecasts, an immense economic impact of HIV/AIDS by the end of the eighties, involving major health-care management problems. Also outside the health-care sector major problems related to the management of HIV/AIDS were envisaged. For example, HIV/AIDS was thought to be a serious threat to the private life-insurance system. In response, specific conditions for HIV-tests of life-insurance applicants were defined [47].

Hay *et al.* [48] were one of the first to provide a detailed estimate of the AIDS-costs distribution over the several health-care sectors. After inpatient hospital care, outpatient hospital resource utilization represented the second largest cost sector with 35% of total health-care costs. Medication - in particular, AZT/zidovudine - is estimated to represent 14% of health-care costs with 10% of costs covered by nursing-home care and the home-care setting, such as district nurse and general practitioner (GP).

Hay *et al.* and other later publications quoted considerably lower cost estimates for the US than the early studies did, ranging from US\$25 000 to 40 000 per person-year [48-50]. In [50] estimated lifetime costs in 1988 amount to US\$57 000. Since then, the same author has produced similar estimates for 1991, 1992 and 1993 [51-53]. Each new estimate surpassed the previous one by approximately US\$20 000. The final 1993-

estimate was US\$119 000, an increase of over 100% in a five-year period and again approaching the cost estimates of the early studies. Scitovsky&Rice [54] compared the costs of treatment and care of AIDS with those of other diseases and causes of death and grimly projected that in 1991 only the total direct costs of car accidents would surpass those of AIDS.

As in the US, the early studies in Europe focused on the hospital costs [55-62]. estimated per person-year hospital costs ranged from US\$22 100 to 46 800 [39]. It was suggested that the treatment of AIDS patients involved somewhat lower costs in Europe than in the US. Information on out-of-hospital care is currently still scarce in the EU, with only tentative estimates of quantitative figures for the Netherlands, Italy and the UK [63-66]. Wiggers&Bergsma [63,64] estimated that in 1988 Dutch direct costs of HIV/AIDS amounted to US\$40 million, with 70% of these costs from prevention, testing and scientific research. At that time hospital costs were estimated at US\$6,7 million of only US\$9,3 million for the total costs of treatment, care and counselling (nursing home, GP, categorical health care services, district nurse, mother's help, psycho-social and psychiatric care). As the epidemic has progressed the patient-related direct costs have obviously increased since then.

In contrast, in Africa and other developing countries the direct costs per case of AIDS are much lower, reflecting the lower gross national product and budgets for health expenditure. However, AIDS is straining an already overburdened health-care system to an extent which is not yet fully clear. Available estimates for African developing countries indicate that annual gross national product per capita (for example, US\$150-300 for Zaïre, Tanzania and Rwanda) is a reasonable proxy for the direct medical costs per patient with AIDS [67,68]. In African countries the number of people progressing to end-stage HIV-disease is escalating rapidly. Hospital services are increasingly burdened due to growing case-loads and budget restrictions. In response to hospital bed shortages, additional costs are being incurred in Africa through the development of AIDS home-care programmes throughout different countries. In countries such as Zambia and Zimbabwe several home care programmes have been established in the beginning of the 1990s [69-71]. Furthermore, projections for Asia show for example that in the year 2000 up to 12 per cent of total hospital bed needs may be for AIDS [72]. As the AIDS epidemics seem to have affected the economically and socially active upper and middle classes disproportionately, the indirect costs are even more relevant than the direct costs and their monetary valuation could exceed the direct costs several times. This has also been illustrated for the developed world [73].

1.4 Scenario Analysis; linking epidemiological models and cost studies

As future epidemiological prospects are at the basis of any economic projection, full economic impact assessments are necessarily preceded by epidemiological modelling. A wide range of models is used for HIV/AIDS [74]. Epidemiological models for quantitatively expressing the HIV/AIDS epidemic can broadly be divided into empirical and population-dynamical models. The former uses surveillance data on AIDS incidence, often in combination with some assumption on progression-of-disease, such as the incubation period. So, empirical modelling is basically the application of statistical methods to AIDS incidence. Empirical models can be further divided into models that project the future AIDS incidence by performing trend extrapolation of AIDS cases and models that estimate the likely HIV epidemic associated with the AIDS figures. The former were used in the early days of AIDS modelling [75-79]. Later the incorporation of information on the natural history of HIV enabled the application of the latter type of empirical models, which are usually referred to as backcalculation models [80-83]. Also, recent estimates of HIV incidence and prevalence and future AIDS incidence by the Paris Centre on the Epidemiological Monitoring of AIDS [84] used the backcalculation approach.

Population-dynamical models explicitly take into account the specific characteristics of the mechanisms that dictate the course of the epidemic [85]. Particular characteristics that population-dynamical modellers are interested in comprise the size of high- and low-risk groups, number of sexual or needle-sharing partners and the infectivity of HIV [86-90]. Some mixed empirical/population-dynamical models have also been used. These mixed models apply the backcalculation procedure within the framework of a population-dynamical model, which implies that successive HIV incidences are not independent but adhere to a postulated functional form [91,92].

An epidemiological projection, by providing estimates of the future pattern of HIV/AIDS incidence, prevalence and mortality, provides the basis for producing socio-economic scenarios. The two main methods for linking epidemiological information with socio-economic data are the *incidence-based* and the *prevalence-based* ones [40]. Incidence-based modelling accounts all future consequences to the year of first occurrence; for example, the lifetime costs for treating and caring for HIV/AIDS are designated to the year of HIV infection. Prevalence-based modelling designates the consequences to the year in which they occur; for example, hospital costs are accounted

to the relevant budget year. In essence, a modelling framework should be designed such that consequences can be expressed according to both approaches or combinations of both [93]. Therefore, the output of the epidemiological models should exceed the basic information on incidence of HIV and AIDS, and be extended to comprise survival, mortality and prevalence. During the spread of HIV/AIDS disease the prevalent case mix has a significant influence on needs for health-care resources. Information on case mix reflects differences in important medical elements (such as diagnosis, prophylactic and late-stage care), treatment patterns, resources (such as inpatient and outpatient care needs) and monetary costs. Furthermore, the case mix should bear a close relationship with severity-of-disease in a patient population. Obviously, different stages of severity require different health-care inputs. In consequence, the investigation of the economic impact of HIV/AIDS involves consideration of multi-dimensional dynamics and uncertainty in basic parameters. The epidemic evolved in societies with changing population distributions (for example, over risk and age groups), rapid developments in medical technology and reforms in the financing and delivery of health care. Furthermore, in a European perspective we are dealing with differences in health-care systems, in the organisation of AIDS care and related differences in resource needs between countries.

The early studies on the economics of AIDS have demonstrated wide variation in costing methods. In order to derive valid cost data at the European level standardization in the methodology of AIDS economic impact studies is needed [94]. The explicit use of a standardized framework for estimation of hospital resources and costs would help improve the quality of methods in resource utilization and cost studies and enhance the comparability of estimates produced, and therefore maximise their usefulness for a range of research and policy purposes at the local, national and multi-national (ie EU) levels [95,96]. Finally, there is a high degree of uncertainty surrounding the economic impact of HIV/AIDS. There is uncertainty about epidemiological developments, impact of prevention, changes in the progression-of-disease due to new therapies and prophylactics and about resource needs in different disease stages. The scenario methodology is chosen as the tool to present the future economic impacts of HIV/AIDS. The technique is designed to deal with multi-disciplinary (biomedical, epidemiological and economic) and multi-national inputs [97]. In addition, it can cope with a high degree of uncertainty by projecting different futures by "if-then" reasoning together with comprehensive sensitivity analysis and analyses of interventions, such as drug therapies.

Scenario analysis emerged during the early 1950s as a technique applied by the Rand Corporation in Santa Monica to military problems. Since then scenario analysis has

become popular in other fields as well [98,99]. Initiated by the Steering Committee of Future Health Scenarios (Stuurgroep Toekomstscenario's Gezondheidszorg; STG) in the 1980s, public health in the Netherlands also became a field for applications of the technique [100]. In 1992 STG published the report on AIDS scenarios in the Netherlands [101-103], which has provided the starting point of this thesis. Previously, scenario analysis was used to investigate the consequences of AIDS in Germany [104]. A scenario is a description of a possible path, governed by a series of developments, leading from the prevailing state of a part of society to a future state, with the goal to gain insight into the mechanisms that determine the path, the future state and the possibilities of influencing these mechanisms [105]. Kahn&Wiener [106] define a scenario as a hypothetical sequence constructed for the purpose of focussing attention on causal processes and decision points. The so-called *reference* scenario is an exploration of the future in which all developments continue their current course. It is an exploration of trends that already exist in society. It might be conceived as a prediction, given unaltered policy. With respect to AIDS we might imagine the reference scenario as a description of the path of the epidemic and the resource-needs implications in an environment in which no new developments (therapeutics, vaccine) or prevention activities occur. Next to the reference, alternative scenarios explore a future in which certain, clearly defined, new developments occur (for example, new AIDS therapies).

1.5 Context

At the initiative of the World Health Organization (WHO), STG commissioned the Netherlands Institute of Mental Health (NcGv) and the National Institute of Public Health and the Environment (RIVM) to conduct a pilot study into the feasibility of a scenario approach to the socio-cultural and economic impact of AIDS on society. This study started in November 1988. Based on the results it was decided to set up a full-scale project, and a scenario committee was appointed. The afore-mentioned NcGv/RIVM research team was responsible for project implementation. The team comprised six persons. Furthermore, two persons of the STG were involved. In developing the Dutch AIDS Scenario project the Program Coordinating Committee on AIDS Research also played a pivotal role. Furthermore, the Chief Medical Officer (GHI) was involved in the project through various consultations of the anonymous register of PWAs in the Netherlands. The final report on the Dutch AIDS scenario project was presented at a

symposium in the Hague in 1992.

At delivery of the Dutch AIDS scenario study, most impact scenarios had been confined to regional and national projections with little use for multi-national projections [107]. In the late-eighties, workshops had been organised by the EU [108,109] and WHO [110] to explore possibilities for the construction of multi-national economic impact scenarios, and a Concerted Action of the EU on this topic started a few years later [111]. The set-up of this multi-national project reflects the involvement of different disciplines in scenario analytic research. Over 50 participants from 30 European universities (European Research Team on AIDS Scenarios) and institutes were assigned to four working groups on epidemiology, modelling aspects, economics and social aspects. A co-ordinating team ensured that the work of an individual working group was tuned to developments in other working groups. The working groups convened half-yearly. Furthermore, all participants met at yearly plenary meetings. The European Research Team on AIDS Scenarios has drawn attention to HIV/AIDS impacts on society through reports and scientific publications [112-114]. In addition, the economic impact of HIV/AIDS at the EU-level was investigated in the related EU-project "Managing the Costs of HIV Infection" (project number SOC 94 20018005F01) [66,95,96]. This project assessed the feasibility of developing a standardized costing framework for HIV/AIDS hospital treatment and care, by investigating the possibilities of applying standardized methods for the collection, processing and presentation of information on resource utilization and costs. Comparable economic information for the different EU-countries is a prerequisite for the construction of multi-national scenario assessments.

Also in the row of International Conferences on AIDS the attention for the economic impact has grown. Where in Paris (1986) only eight abstracts [115-122] were directed at the economic impact, at the Vancouver Conference (1996) 24 abstracts were classified as referring to the economic impact and over 50 abstracts were classified as addressing health care costs/direct costs/hospital costs. Finally eleven abstracts involved the projection of costs. Furthermore, a substantial number of abstracts addressed the cost-effectiveness of various interventions, treatments and medication (for example HIV-screening of pregnant women, intensive case management and combination triple-therapy). At the Oslo conference (1988) for the first time three abstracts were explicitly directed at cost projections [123-125]. In Montreal (1989) the scenario-analytic approach was specifically introduced [126], 24 abstracts were classified as economic impact and 2 involved cost projections [127,128]. In San Francisco (1990) the Dutch application of the scenario-analytic approach to the economic impact of AIDS was presented for the first

time [129]. In the next years in Florence (1991) and Amsterdam (1992) the Dutch research team presented several abstracts on scenario analysis for AIDS impact in the Netherlands [130-135]. In Amsterdam (1992) the number of abstracts on direct/health care/hospital costs, economic impact, cost projection and scenario analysis reached its current maximum with almost 100 abstracts. In Vancouver (1996) the multinational reference scenario on the economic impact was presented in a set of four abstracts [136-139].

The types of investigations pursued in this thesis should come up with information that is relevant for health-care policy making. Obviously, costing aspects are a concern of health-care policy and information about the costs of a new and spreading disease such as HIV/AIDS informs decision makers about the size of the problem. Current estimations of this size and future projections thereof give a basis for allocating budgets, capacities and funds. Also beyond the health-care sector such estimations and projections are of relevance, for example in marketing pharmaceuticals and impacts on life-insurance markets. Furthermore, sound costing analysis is basic to any cost-effectiveness approach in the field of HIV/AIDS. Important emerging questions on whether or not to screen sub-populations for HIV, to apply very costly triple therapies to different exposure groups or to set-up/intensify prevention programmes can only be adequately addressed from an economic point of view if good cost estimates for the present and future are available.

1.6 The Objectives of the Thesis

This thesis highlights the important issues that emerge in attempts to move on from the use of scenario analysis at the national level to the multi-national (EU-)level. In particular, the thesis focuses on the projection of hospital resource needs and corresponding costs of HIV-infected persons in the Netherlands and the EU by the end of the century. The specific objectives are:

- 1 To develop a standardized methodology for the estimation of HIV/AIDS-related personal health-care costs, to allow valid comparisons between economic impact studies performed at different times, in different research settings and in different countries;
- 2 To develop methodological quality criteria and applying these criteria to identify economic impact studies in various European countries, that provide high-quality basic data for multi-national scenarios;

- 3 To develop a disease-staging model that reflects relevant differences in resource needs and costs;
- 4 To develop a general framework for linking epidemiological modelling and economic impact in a scenario-analytic approach that encompasses further methods to deal with uncertainty (confidence intervals and sensitivity analysis);
- 5 To estimate the economic parameter values in mixed epidemiological/economic models for impact assessment and scenario analysis relating to future needs for hospital resource utilization and corresponding costs;
- 6 To project the consequences for health-care resources and costs of potential future trends in the epidemic in sets of future scenarios and to relate these projections to national estimates of health-care resources utilization and costs;
- 7 To construct a generic/standardized approach to allow comparison of future projections of HIV/AIDS health-care impacts between countries and with other diseases;
- 8 To identify differences in AIDS care between EU-countries and to relate these differences to variations in characteristics of health-care systems;
- 9 To support the development of health-care policy in the field of HIV/AIDS at the national and multi-national EU-level, ie to inform policy makers on costing aspects;
- 10 To contribute to health-economics science in developing a dynamic cost-of-illness approach, viz an approach for estimating cost-of-illness of infectious diseases; and
- 11 To provide the basis for cost-effectiveness analysis in the field of HIV/AIDS and infectious diseases in general.

1.7 Outline of the Thesis

As a first illustration and as a basis for the more recent work, chapter 2 presents PYLL per 1000 population in three EU-countries. Trends for AIDS incidence are projected using an "early-type" empirical model, assuming a constant future growth rate. Therefore, chapter 2 serves as a motivation for scenario analysis enabling more than just projecting current and recent courses by incorporating knowledge from different research fields. In chapters 3 and 4 data gathering and data evaluation for scenario analysis at the Dutch and EU-level are presented. In addition, chapter 4 shows the development and application of a population-dynamical model to the epidemic in the EU as a whole. Some preliminary

scenarios on hospital bed needs and costs for 1995 are presented. Chapter 5 provides the results on scenario construction for the Netherlands, in particular for resources and costs in the hospital sector. The annex to this thesis provides the background for chapter 5 its comparison of HIV/AIDS hospital bed needs projections with those for other diseases. Based on a specific research request from the State Secretary of Health, chapter 6 extends chapter 5 its results to non-health-care sectors, in particular to the life-insurance sector. The discussion of national scenario analysis in chapter 7 illustrates the importance of an appropriate staging of HIV/AIDS for health-care resource needs. Furthermore, this chapter discusses the importance of a standardized approach to estimating HIV/AIDS costs in the different EU-countries. In chapters 8 and 9, the scenario-analytic approach is extended to the EU-level. In particular, chapter 8 provides the reference scenario at the global EU-level by connecting information from databases on AIDS hospital resource utilization in six EU-countries to recent empirical projections of future AIDS incidence produced by the European Centre for the Epidemiological Monitoring of AIDS in Paris. From this, future scenarios on hospital care for the EU as a whole have been produced. Chapter 9 presents the details on AIDS hospital care for several EU-countries. Also, this chapter tries to relate differences in AIDS hospital care in two selected countries to the respective characteristics of the health-care systems. Finally, chapter 10 concludes the thesis with discussions and the main conclusions.

Chapter 2

AIDS Impact Scenarios; questions for the years to come

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It is generally agreed that research to support the fight against AIDS requires an international and inter-disciplinary approach to the broad range of problems emerging from the three successive epidemics: (1) infection with HIV (2) the occurrence of AIDS and other HIV-related conditions and (3) the epidemic of socio-economic consequences of HIV infection and AIDS [140]. Since it has become clear that AIDS will be more than a short-term challenge to biomedical scientists, coping with social, psycho-social and economic impacts may be considered an important health-policy issue. Recently, the Council of the European Communities (EC) and the Ministers of Health of the Member States stressed the importance of, research into and evaluation of socio-economic impact [1].

Analyses of the third epidemic are demanded, including impact forecasts and scenarios. Two EC-activities prepared the ground for co-ordinated research in this field: the Concerted Action on the Statistical Analysis and Mathematical Modelling of AIDS (Bilthoven workshops 1986 [141,142], and the Study on Economic Aspects of AIDS and HIV Infection (Munich workshop, 1989 [109]). Both 1989 workshops began to explore impact scenarios and the perspective for linking models for HIV transmission with socio-economic information. Here some preliminary results are presented of a collaborative (Netherlands, FRG, France) study on short-term forecasts concerning the impact of AIDS compared with a number of other death causes liable for prevention. As one indicator for the social burden of diseases, potential years of life lost (PYLL) are used. PYLL are defined as the remaining life expectancy at time of death; here, 1985 data were used (sources: Centraal Bureau voor de Statistiek, Statistisches Bundesamt, Institut National de la Santé et de la Recherche Médicale). PYLL are reported per 1000 population.

Figure 2.1 shows observed and projected trends of PYLL due to AIDS and due to infectious diseases other than AIDS (ICD 001-139), lung cancer (ICD 162), road traffic accidents (ICD E810-819) and suicide (ICD E950-959). PYLL due to AIDS are based on the surveillance of AIDS cases by date of diagnosis (WHO Collaborating Centre on AIDS, Paris), adjusted for reporting delay [143] up to June 30st 1989, the observed age distribution of AIDS cases, and an assumed survival time of 1.5 years after diagnosis. Trends for AIDS cases are projected assuming a constant growth rate equal to the observed rate during the last 3 years, for the respective countries. The present procedure is held to give reliable forecasts only for the short-term (2-3 years). Trends for other death causes are based on mortality data registered over the period 1980-1987 and are

projected by linear extrapolation of the observed data.

The three countries show rather similar patterns: stable or slowly changing PYLL due to infectious diseases, lung cancer and suicide, decreasing trends for road accidents, and an increase for AIDS. In a few years, PYLL due to AIDS tend to exceed those due to other infectious diseases. They come close to other death causes before 1995. As a first hypothesis on future trends, extrapolations were also projected beyond what statistically would be considered reasonable in terms of confidence limits (grey areas). A detailed discussion of methods and results is presented elsewhere [144]. The techniques are already useful in ranking risks and in communications between researchers and policy makers. In view of the uncertainties and gaps that were met when trying to produce reliable impact forecasts and scenarios of possible futures, only research priorities are focussed on. One is confronted with two kinds of gaps - gaps with respect to data and gaps with respect to methods.

Fig 2.1

Observed and projected (grey areas: long-term projections beyond confidence limits) potential years of life lost (PYLL) per 1000 population for AIDS (line), infectious diseases (short dashes), lung cancer (long dashes), suicide (alternating dashes), road accidents (dots)

Gaps in data concern epidemiological and behavioural aspects of the transmission and prevalence of HIV infections. These have been specified by model-builders and are well-known in the literature [145]. The main information source of the epidemic is still the surveillance of AIDS cases; but should AIDS incidence be the focus in the context of improving medical care [126]? Early interventions could influence the progress of the disease in individuals and affect the number of people to be cared for in the different stages of the disease. Consequently, for impact assessment, the prevalences in the different stages of the disease are needed as an epidemiologic basis; yet, they are not available. Even for the actual number of infected in developed countries, only vague estimates are available. For seemingly simple indicators such as the survival time of AIDS, another important impact determinant, accurate data are currently lacking. The same is true for the pre-AIDS stages. Economic impact data is also too scarce to describe the situation comprehensively. Studies [109] tend to be incomplete in terms of sectors of care covered, time span included, and disease stages dealt with. Often, studies only refer to hospital costs for full-blown AIDS at one point in time. Also one has very little empirical knowledge about the extent of actual utilization of our health-care systems. For the quantitative study of impacts, we are just beginning to learn how much we do not know. Referring to all three epidemics - HIV, AIDS and socio-economic impact - conferences clarified essential gaps in methodology.

International and inter-disciplinary work - between disease modellers, epidemiologists and economists are a necessary condition for work on scenario construction. Comparable data collection in epidemiological and impact studies is one of these communication issues. Methodologically, tools for complex reasoning are required to link epidemiology and economics.

In the light of these problems, the preliminary nature of this attempt to measure the future short-term impact of AIDS is stressed. Systematization of procedures for data gathering, and development of methods to build scenarios referring to the three epidemics simultaneously, are urgently needed for the development of health policy.

Chapter 3

A Comparison and Integration of Studies on HIV-related Hospital Resource Utilization and Costs; towards economic scenarios for the Netherlands

The Dutch version of this chapter was published by MJ Postma, MGW Dijkgraaf, JCC Borleffs, DP Reinking, FMLG van den Boom, JC Jager in *Tijdschrift voor Sociale Gezondheidszorg* (1992, 70:189-96); reprinted with permission

Summary

The results of *three Dutch studies* on the economic impact of HIV infections and AIDS for the hospital are compared. All three studies involve a co-operation between a hospital and a research centre. Even after data have been converted to similar dimensions results differ. This can be attributed to several factors, related to for example the operationalization of the term "costs" and characteristics of the patient population. Discussing these factors the possible significance of the results, especially with regard to use in prediction and scenario analysis, is treated. The comparison renders information which can be linked to epidemiological modelling for impact assessment. The studies indicate that in the CDC-IV stage hospital inpatient days per person-year range from 51.1 to 58.4. Hospital costs per person-year of CDC IV are f36 300 (SZ/KPMG) and f46 800 (AZU/RIVM). Results suggest that homosexual men generate higher costs and bed needs per person-year of CDC IV than intravenous drugusers. For building future scenarios the point of departure in 1990 has been established: (1) the need of hospital beds for CDC IV halfway 1990 is 146 beds based on data from AZU/RIVM and 150 beds based on SZ/KPMG; (2) hospital costs for CDC IV amount to f37 million (AZU/RIVM) and f28 million (SZ/KPMG); (3) hospital costs for all stages are estimated f44 million based on data of AZU/RIVM. For scenario analyses an integration of methods from the studies discussed in this paper would form the optimal source of information at the moment: longitudinal research into the amount and type of care linked to estimates of the cost prices of the several activities.

List of Abbreviations to Chapter 3

AZU	Academisch Ziekenhuis Utrecht / University Hospital Utrecht
AZUA	Academisch Ziekenhuis van de Universiteit van Amsterdam / Teaching Hospital of the University of Amsterdam
KPMG	KPMG Klynveld Management Consultants
NIPG	Nederlands Instituut voor Praeventieve Gezondheidszorg / Netherlands Institute for Preventive Health Care NIPG-TNO
SZ	Slotervaart Ziekenhuis / Slotervaart Hospital
COTG	Central Board for Health-care Tariffs / Centraal Orgaan Tarieven Gezondheidszorg

3.1 Introduction

The Dutch AIDS scenario analysis started in the summer 1990 on the initiative of WHO and STG. The project "Scenario analysis of the socio-cultural and economic consequences of AIDS for the Netherlands" was carried out by the Netherlands Centre for Mental Health (NcGv: Nederlands centrum Geestelijke volksgezondheid) and RIVM. This paper on the impact of the AIDS epidemic on hospital resource utilization is based on the research within the framework of the project into the economic consequences.

At a macro level, the costs of hospital care are yet but a small percentage of the total direct and indirect costs of the HIV and AIDS epidemic [63,64]. The importance of insight into the resource utilization and corresponding monetary costs of inpatient care for HIV-infected people is particularly relevant at a meso level and for future years. The more the epidemic spreads, the more important the regional and national planning of hospital resources and the detection of financial bottlenecks will become [146].

To date there have been three Dutch studies investigating the impact of the HIV/AIDS epidemic on hospital resource utilization and corresponding monetary costs. The studies carried out by the Netherlands Institute for Preventive Health Care (NIPG) in collaboration with the Teaching Hospital of the University of Amsterdam (AZUA) [60,61,147], and that carried out by KPMG Klynveld Management Consultants (KPMG) in collaboration with the Slotervaart Hospital (SZ) in Amsterdam [148-150] have been finalized. The study by the University Hospital of Utrecht (AZU) in collaboration with the RIVM in Bilthoven [58,151-153] is a long-running project and is still in progress.

The studies differ in their design and emphasis. Also they are not solely restricted to hospital resource utilization and corresponding costs:

- the AZUA/NIPG-study examines, in addition to hospital costs, those of outpatient care, research, prevention and the indirect costs (absenteeism, years of life lost);
- the AZU/RIVM-study also focuses on the assessment of the effectiveness of care and trends in resource utilization and costs *in time*; and
- the SZ/KPMG-study examines the *extra* costs of hospital care - defined as the difference between the incurred costs and the budgeted costs of care and treatment - for the purpose of assessing the need for extra financing facilities for AIDS hospitalisations.

The aim of this study is to determine reference values for parameters by comparing and integrating the results of the different studies. These values are needed to make short-term forecasts and scenario analyses of resource utilization (future bed needs)

and total hospital costs. The following sections describe the characteristics of the studies, as well as results considered relevant to scenario analysis. To facilitate comparison of the studies, some of the data are re-calculated in that they can be presented in the same dimensions. The results of the different studies are discussed with regard to aspects of the methodology and design of the individual studies, such as the composition of the study population, the use of cost prices instead of charges, etcetera. It will be made clear that the parameter estimates should be used with care for both current estimations and scenario analyses. The last section gives an overview of the recommendations for the design of future research. This study should provide a step towards the aims of WHO and the EU that internationally comparable methods should be used for the calculation of the economic consequences of the HIV/AIDS epidemic [66,154].

Table 3.1 *Registration period, study approach, design, setting and site of three Dutch studies into the impact of AIDS on hospitals*

AZUA/NIPG	AZU/RIVM	SZ/KPMG
1982-88	1987-present	1989
Retrospective	Prospective	Prospective
Longitudinal	Longitudinal	Cross-sectional
University hospital	University hospital	General hospital
Amsterdam	Utrecht	Amsterdam

3.2 Study Characteristics and Basic Data

Study characteristics that are relevant to hospital resource utilization and monetary costs are given in Table 3.1. The AZUA/NIPG-study is retrospective, with longitudinal collection of data over the period January 1982 through to spring 1988 (6.5 years). Data were collected in a teaching hospital in Amsterdam. The AZU/RIVM-study started in 1987 and is prospective (directed data collection during the period of conducting the study). The study design is longitudinal, and data are collected at the University Hospital Utrecht. The SZ/KPMG-study is prospective with a cross-sectional design and was carried out in a general hospital in Amsterdam. Data were collected in the spring of 1989 (5.5 months).

Table 3.2 provides information about the length of the registration period, the composition of the patient populations according to the classification of HIV infection by the CDC [16,17], the total number of observation-days, and the total costs generated (inpatient and outpatient care and treatment). The definition of the term *cost* used in the

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different studies will be discussed later.

Table 3.2 *Length of registration period (in years), number of patients, number of observation days and total hospital costs (in guilders)*

	AZUA/NIPG*	AZU/RIVM	SZ/KPMG
Registration period	6.5	2	0.45
Patients			
CDC II	-	21 (-4) [®]	16 (-1)
CDC III	195 (-195)	15 (-1)	1
CDC IV	230	21	63
All stages	230	52	79
Observation days			
CDC II	-	4753	1710
CDC III	57 340	6034	156
CDC IV	77 240	5125	7023
All stages	134 580	15 912	8889
Total costs (f)			
CDC II	-	65 000	43 000
CDC III	-	70 000	800
CDC IV	-	657 000	699 000
All stages	15 640 000	792 000	743 000

* For this study the table reflects the data for patients with AIDS (CDC IV) and for those in the pre-AIDS stages (CDC II); [®] The numbers in parentheses represent patients diagnosed as CDC IV (or AIDS) during the registration period.

In the AZUA/NIPG-study data refer to 230 patients, all of whom diagnosed as having AIDS according to the surveillance case-definition [7,8]. Data on resource utilization and costs generated by 195 patients (85%) in the pre-AIDS stage are included in the total. The registration period is 6.5 years, and during this time 134 580 observation-days are counted. The number of observation-days of a patient is the time between the first contact with the hospital (for HIV-related purposes) and the moment when the hospital loses contact with the patient, due to change of hospital or death. The total costs calculated during the registration period amount to f15 640 000.

Up to the end of 1988, the patient population of the AZU/RIVM-study consisted of 21 patients with asymptomatic HIV infection (CDC II), 15 patients in CDC stage III, and 21 patients in CDC stage IV. Four of the CDC-II patients and one of the CDC-III patients

developed stage IV symptoms during the study period, covering 1987-1988. So, the total number of patients during the study period is 52¹. During this 2-year period nearly 16 000 observation-days are counted — 4753 for CDC-II patients, 6034 for CDC-III patients, and 5125 for CDC-IV patients. The total costs are f792 000, of which f657 000 is for CDC-IV patients, f70 000 for CDC-III patients, and f65 000 for CDC-II patients.

The SZ/KPMG-study involves 79 patients. At entry, 15 Patients are classified in CDC stage II, 1 patient in CDC stage III, and 63 patients in CDC stage IV. One CDC-II patient developed symptoms consistent with CDC IV. The registration period is 0.45 year (165 days), and the total costs are f743 000 for 8889 observation-days. The distribution of costs over the various CDC stages is f43 000 for 1710 observation-days of CDC-II patients, f800 for 156 observation-days of the CDC-III patient, and f699 000 for 7023 observation-days of CDC-IV patients.

3.3 Comparison of Study Results

Table 3.3 gives an overview of the hospital costs for patients with HIV infection by CDC stage. The average costs are expressed per observation-year and indicate the costs that an average patient would generate in a full year of observation. Expressing costs in terms of observation-years is preferred because the length of the observation-period can be eliminated as an explanation for any differences observed. This choice of representation is consistent with that used internationally [156].

The AZUA/NIPG-study includes only those patients who finally developed AIDS, whereas 60% of the patients in the AZU/RIVM-study and 20% of the patients in the SZ/KPMG-study are not classified as CDC IV. It is not possible to calculate costs per CDC stage on the basis of the data in the AZUA/NIPG-study. The costs per observation-year for AIDS patients will be higher than the f42 500 mentioned in the AZUA/NIPG-study, given that AIDS patients cost more per observation-year than pre-AIDS patients.

Remarkably, both the AZU/RIVM and the SZ/KPMG studies show hospital costs to be lower for CDC-III patients than for asymptomatic CDC-II patients. This might be explained by the costs of the one-off diagnostic examinations to determine the medical history of the patient.

Only the AZUA/NIPG-study provides data about the lifetime costs of AIDS. A group

¹ At the end of June 1990 there were 126 patients in the study. Data gathered up to June 1990 were presented at the International AIDS Conference in Florence [155].

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of 127 patients could be formed for whom the entire course of the illness, from first contact with the hospital for symptoms of HIV infection to death, falls within the registration period. The costs are f87 000 per patient.

Table 3.3 *Hospital costs per person-year in guilders (f)*

	AZUA/NIPG	AZU/RIVM	SZ/KPMG
CDC II	-	5000	9200
CDC III	-	4200	1900*
CDC IV	-	46 800	36 300
All stages	42 500	18 200	30 500

* Data from one patient only.

Table 3.4 gives an overview of the average resource utilization per observation-year in terms of the number of admissions and the number of inpatient days. The resource-utilization data for HIV-infected patients during the period in which they were classified as CDC IV are given in parentheses. These data can be used to project future bed needs.

Table 3.4 *Amount of care for HIV-infected persons (CDC-IV patients in particular) in terms of number of admissions per person-year, inpatient days per person-year and length of stay (inpatient days per admission)*

	AZUA/NIPG	AZU/RIVM	SZ/KPMG
Admissions	1.9	0.8	2.6
Inpatient days	37.4 (58.4*)	17.2 (51.1)	44.4 (52.5)
Length of stay	19.4	20.7 (23.1)	17.4

* AIDS.

Analysis of the data for the above-mentioned 127 patients in the AZUA/NIPG-study show that, during the full course of the illness, HIV-infected patients are admitted more than three times on average, with a total of 77 inpatient days. The average length of stay is 23.3 days. So, the patients who died were hospitalized longer than the patients who were alive at the end of 1988.

Comparison of the studies, ignoring the CDC classification of the patient population, shows that the average costs per observation-year vary between the studies, from f18 200 (AZU/RIVM) to f42 500 (AZUA/NIPG). Even when calculated per CDC stage,

still a substantial variation in costs between studies remains.

Although the average length of stay shows only a small variation (17.4 days to 20.7 days), the average number of admissions per observation-year varies between 0.8 en 2.6, and the average number of inpatient days per observation-year varies between 17.2 days and 44.4 days. The variation in the number of inpatient days per observation-year of CDC-IV/AIDS is much smaller: 51.1 to 58.4.

3.4 Integration of Study Results

There are several factors that can explain the differences between the study results. A factor that is typically related to the methodology used is the *operationalization of costs and different types of costs*. The operationalizations of the costs used in the studies are given in Table 3.5, and discussed below for the costs of care during an inpatient day.

Table 3.5 *Operationalization of costs per hospital activity: charges based on national health tariffs, estimated cost prices and prices paid by the hospital to third parties*

Activity	AZUA/NIPG	AZU/RIVM	SZ/KPMG
Artificial ventilation	Charges	Charges	Cost prices
Blood transfusion	Charges	Charges	Cost prices
Consultation	Charges	Charges	Cost prices
Diagnostics	Charges & prices	Charges & prices	Cost prices
Medication	Prices	Prices	Prices*
Inpatient day	Charges	Cost prices	Cost prices

* Retail price plus overhead for the pharmacy.

The AZUA/NIPG-study uses mainly charges from the National Health Tariffs Authority (COTG: Centraal Orgaan Tarieven Gezondheidszorg; all-in charges, so that most common specialist treatments are included), with the exception of diagnostic examinations and drugs prescribed by third parties but charged to the AZUA. The charge per inpatient day varies between f692 and f780 (average: f740), depending on the utilization of intensive care.

The AZU/RIVM-study uses both COTG charges and prices (both cost prices and prices paid by the hospital). The estimated cost price per inpatient day varies between f261 and f848, depending on the daily intensity of care (low, medium, high, intensive care). This cost price includes the necessary care provided by nurses, internists, and their

assistents. For the period 1/1/87 to 31/12/88 the average cost of care per inpatient day was f483.

The SZ/KPMG-study makes as much use as possible of pre-calculated cost prices. The cost price of care during an inpatient day is on average f289, depending on the intensity of care (the operationalization of this term is different from that of the AZU/RIVM-study). This cost price included the daily use of medical means, nursing, and appropriate overhead costs.

The use of charges rather than pre-calculated cost prices leads to overestimation of the costs of an inpatient day and to underestimation of the costs of diagnostic examinations and other interventions. In practice, the COTG charges for inpatient care are used to adjust hospital finances once the external budget has been determined. There is no one-on-one relationship to the real costs of an inpatient day and, as a result, the relative influence of different types of costs on the overall cost of an inpatient day is unclear.

Besides this distinction between charges and (cost) prices, the selection of the types of costs included determine what is understood by "hospital costs". All of these studies omit certain types of costs. For example, none of the studies explicitly takes the costs of interest and depreciation into consideration. Both the SZ/KPMG and AZU/RIVM studies take most of the material costs into consideration. The SZ/KPMG-study explicitly includes personnel overheads and the costs of training. If the AZU/RIVM-study were to take these costs into account, then the figures given in Tables 3.2 and 3.3 would have to be adjusted upwards. At the moment it is not possible to determine the extent of this adjustment. In the AZUA/NIPG-study, these types of costs, as well as interest and depreciation, are implicitly included in the charge per inpatient day.

The studies also differ with respect to the *reference year* on which all costs are based. The AZUA/NIPG-study uses 1988 prices, the AZU/RIVM 1987/1988 prices, and the SZ/KPMG-study 1989 prices. However, these price differences will have little impact on the data.

The *time and site* in which the research is carried out are factors that could also contribute to the differences in the costs and resource-utilization data. The time periods when the studies were carried out are not completely the same. In contrast to the AZU/RIVM and SZ/KPMG studies, the AZUA/NIPG-study includes data from the early phase of the epidemic in The Netherlands. Only the last 1.5 years of the registration period are the same as in the AZU/RIVM-study. The AZU/RIVM and SZ/KPMG studies are more similar with regard to the study period. Thus the study period (especially with regard to changes

in treatment strategies) will have had similar effects on the results of the two most recent studies.

The conduction of two of the studies (AZUA/NIPG and SZ/KPMG) took place in Amsterdam, the third (AZU/RIVM) in the Utrecht-region. Because the first cases of HIV and AIDS occurred in Amsterdam, Amsterdam functioned as a national AIDS centre, certainly in the beginning of the epidemic. Up to 1987 patients throughout the Netherlands were referred to Amsterdam. Expertise in inpatient and outpatient care probably developed faster in Amsterdam than elsewhere, with consequences for resource utilization. For example, better developed outpatient services reduces demand for inpatient services, which could have lowered the resource utilization and costs of both Amsterdam studies relative to those of the AZU/RIVM-study.

In addition, time and site refer directly to differences between hospitals in the *protocolling* of care and treatment. Experience, new insights, and the availability of outpatient services leads to differences in the protocols, which in turn are related to the amount and costs of care. The results of these studies bear a strong relation to the way in which care and treatment were provided by the hospitals involved.

The SZ/KPMG-study has explicitly described the protocols for treatment and care to be used in the hospital [150], under the concept of "good practice". However, this "good practice" can deviate from the care and treatment generating the cost and resource-utilization data reported.

Other influencing factors of importance are the *size* - which is also partly dependent on the duration of *follow-up* - and the *composition* of the patient population. The size of the patient population and the duration of the follow-up period indicate to what extent study results are representative. There was quite a large difference among the three patient populations with respect to size (52 to 230 patients) and to the total number of days the patients were monitored (8 889 to 134 580 observation-days, Table 3.2). The AZUA/NIPG-study had 4.5 more patients and 9 times the number of observation-days than the AZU/RIVM-study, and 3 times more patients and 15 times more observation-days than the SZ/KPMG-study. The SZ/KPMG-study had few observation-days for the pre-CDC-IV stages. Clearly, the results of the AZUA/NIPG-study are most likely to be representative ones.

The composition of the population with regard to the various *risk groups* can also affect the results. Table 3.6 shows results of the SZ/KPMG-study for homosexual men and intravenous drug users. Per observation-year, intravenous drug users are more expensive and require more inpatient days than homosexual/bisexual men in the CDC-II stage. This

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relationship is reversed in CDC-IV patients, although it should be borne in mind that eight CDC-IV homosexual men died during the study, and that the relatively high costs of providing care for these patients in the terminal stages are included in the data. In the SZ/KPMG-study, the costs of care *per patient* are nearly three times higher for the patients who died than for the patients who stayed alive (all CDC stages). No intravenous drug users died during the study period. The data shown in Table 3.6 seem to contrast data from the US that intravenous drug users generate higher costs than homosexual men, because the latter have a better developed social support network [157]. In general, at the moment one does not know to what extent the socio-economical background of a risk group influences costs and resource utilization.

Table 3.6 *Number of observation days, inpatient days and costs (in guilders) per person-year for homosexual men and intravenous (iv) drug users (including homosexual intravenous drug users) per CDC stage*

CDC-stage	Risk group	Observation days	Inpatient days	Costs (f)
II	homosexual men	689	4.2	5700
	iv drug users	468	33.5	14 100
III	homosexual men*	156	0	1900
	iv drug users	0	-	-
IV	homosexual men	5992	47.9	34 800
	iv drug users	633	16.1	15 300
All stages	homosexual men	6837	42.4	31 100
	iv drug users	1101	23.5	14 800

* Data from one patient only.

Source: SZ/KPMG.

There are relatively fewer intravenous drug users in the AZU/RIVM-study population (accounting for 5.3% of the total number of observation-days) than in the SZ/KPMG-study (accounting for 12% of the total number of observation-days). The number of intravenous drug users in the AZUA/NIPG-study population is not known.

The patient populations of the three studies can also be distinguished in terms of the proportion of patients who *died*. In the AZUA/NIPG-study, 65% of the patients died during the registration period, as compared to 17% in the AZU/RIVM-study, and 11% in the SZ/KPMG-study. Given that the patients who died generated, on average, higher costs than the patients who stayed alive during the study period - because of the high costs of terminal care - it is expected that the per observation-year costs of AIDS in the AZUA/NIPG-study is higher than those of the two other studies.

3.5 Concluding Remarks

With regard to the specific field of hospital care, three Dutch studies which pay attention to the amount and costs of care and treatment were analyzed. The studies report different data on resource utilization and costs, which can be explained by various aspects of the methodology and design of the individual studies. These explanations should be borne in mind when determining parameter estimates for impact assessment and scenario analyses.

The three studies each have advantages and disadvantages with regard to application in scenario analysis. The AZUA/NIPG-study has the advantage of a large population (large number of observation-days), but the disadvantages that it might be outdated (protocols and clinical practice have changed) and that it uses all-in charges throughout. The SZ/KPMG-study has the advantage that cost prices were consistently used to determine costs, but the disadvantage of a relatively short observation-period (few observation-days for pre-CDC-IV stages). The AZU/RIVM-study has the advantage of a longitudinal design (increasing number of observation-days, making it possible to determine trends) but, as yet, only makes partly use of cost prices.

The results of these studies can be used within the framework of the scenario project to determine the number of beds needed and the total costs of hospital treatment and care for HIV-infected people on a national basis, in the present and in the future. By linking estimates of the number of inpatient days per observation-year of AIDS and per observation-year estimates of hospital costs to output for 1990 of available epidemiological models [23,144], illustrations of these calculations are gained:

- on average, 146 beds were needed for CDC-IV patients on any day in 1990 on the basis of the AZU/RIVM data, and 150 beds on the basis of the SZ/KPMG data, applying a bed occupancy of 75% [158];
- hospital costs of CDC-IV patients were f37 000 000 in 1990 on the basis of the AZU/RIVM data, and f28 000 000 on the basis of the SZ/KPMG data; and
- hospital costs of patients in all stages were f44 100 000 in 1990 on the basis of the AZU/RIVM data [131].

The AZUA/NIPG data do not allow us to differentiate costs per CDC stage, refer to a previous phase of the epidemic and are therefore less suitable for these type of calculations.

The difference between the costs of care for CDC-IV patients in the three studies is noteworthy. Besides the other factors mentioned, the use of cost prices (SZ/KPMG-study) versus a combination of cost prices and charges (AZU/RIVM) is responsible for this

difference. From a methodological point of view, estimates based on cost prices are to be preferred (SZ/KPMG-study). However, because of the limited number of observation-days for pre-CDC-IV stages in the SZ/KPMG-study, calculations of the costs of all stages were based on the data from the AZU/RIVM-study alone.

The SZ/KPMG- and AZU/RIVM-studies gave very similar estimates of the bed needs for CDC-IV patients. Both studies reported a similar number of observation-days for CDC-IV patients, and the definitions of the term inpatient day were unequivocal. Hence, the bed requirements can be determined with some degree of certainty.

For future years much can change in the hospital care and treatment of HIV-infected persons. For this reason it is important to monitor and analyse the costs, and amount and type of treatment and care against a background of certain distinct developments [130]:

- the changing composition of the patient population;
- increasing use of early intervention;
- other developments in medical technology and the associated increasing survival; and
- the shift in the relationship between in-patient and out-patient care.

This makes it possible to adjust the parameters used for calculations in future scenarios. The most recent data available from the AZU/RIVM-study show a drastic reduction in the number of inpatient days per observation-year [159], which will have direct consequences for future bed requirements.

Bearing this in mind, an integration of the methodologies used in the above studies would seem to provide an optimal source of data for scenario analyses, namely, longitudinal research into resource utilization combined with cost-price estimates of the various components of care and treatment.

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Chapter 4

Economic Impact of the AIDS Epidemic in the European Community; towards multi-national scenarios on hospital care and costs

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Summary

Objective To underpin multi-national public-health HIV/AIDS planning in the European Community (EC) by integrating national studies on HIV/AIDS in scenario analysis.

Data & Methods Three types of data are used: routine surveillance-data, information on disease progression and observational studies on the economic impact. The HIV/AIDS epidemic is simulated using two models (MIDAS and PC-based AIDS Scenarios). Selected simulations, consistent with surveillance data, are connected to economic impact (hospital bed needs and annual hospital costs for AIDS patients). Parameter values expressing per person-year economic impacts are derived from a structured review of publications on economic aspects of HIV/AIDS.

Results Evaluation of published studies on hospital resource utilization and costs in EC-countries shows that there are significant differences between both countries and studies, even after conversion to similar measures (for example, using purchasing power parities). These differences are partly due to factors such as the composition of the patient population and differences in methodology. Economic impact is analysed for combinations of three factors: survival time after AIDS diagnosis, hospital inpatient-days needed per person-year and corresponding per person-year hospital costs. All scenarios indicate 1995 hospital bed needs above the 1990 level of 5400 beds. Hospital cost projections for 1995 vary (up to US\$1050 million).

Conclusions (1) For economic impact assessment, there are important data gaps in epidemiological and economic areas, and in the methods for linking these. (2) Standardization of studies on resource utilization and costs of HIV/AIDS is necessary to provide a sound basis for multi-national scenarios. (3) Preliminary multi-national scenarios show that by 1995 hospital bed needs for AIDS might reach 0.45 % of all hospital beds available in the EC, and that hospital cost projections for AIDS in that year will range from 0.15 % to 0.30 % of EC health-care expenditure.

Sponsorship

This research resulted from two activities co-ordinated and sponsored by the EC (the Concerted Action on Statistical Analysis and Mathematical Modelling of AIDS and the European Study on Economic Aspects of AIDS and HIV Infection). The STG and WHO also contributed to the international co-operation on AIDS scenarios.

4.1 Introduction

Research to support the fight against AIDS has become inter-disciplinary. Coping with the broad range of socio-economic impacts is considered a significant health-care policy issue, since it has become clear that AIDS is more than a short-term challenge for the basic sciences. The importance of studying socio-economic impacts has recently been emphasized within the EC [1]. This study develops and applies methods to construct scenarios on the economic impact of AIDS, through the integration of mathematical models and three types of information: (1) routine surveillance-data on AIDS incidence; (2) data on disease progression; and (3) information from observational studies on economic impacts.

Co-ordinated research linking epidemiological models and socio-economic information (i.e., exploring impact scenarios) results from two EC-activities: the Concerted Action on the Statistical Analysis and Mathematical Modelling of AIDS (Bilthoven workshops 1986 [141,142], 1988, 1989 [108] and 1992) and the Study on Economic Aspects of AIDS and HIV Infection (Munich workshop, 1989 [109]). The needs and constraints of developing an integrative approach have been discussed elsewhere [152,160]. Earlier work [144] considered the use of both a statistical and a simulation technique to model the past, present and future impacts of the HIV/AIDS epidemic. Impact assessment was illustrated by extrapolation of potential years of life lost in three countries of the EC.

This study focuses on: (1) a description of the epidemiological data and models to be used; (2) a review of available EC-studies on hospital bed utilization and corresponding costs, together with an assessment of the problems involved; (3) preliminary scenario results, with projections of hospital costs and number of hospital beds needed for full-blown AIDS patients in the EC; and (4) an outline of future requirements concerning collection and comparison of impact data with regard to scenario analysis, resulting in guidelines for the standardization of collection.

The approach advocated and applied here contributes to the integration of national studies and will be useful for public-health strategy development at a multi-national level. This study should contribute to the EC objective adopted by all member states to continue the fight against AIDS and, as a possible future objective, contribute to a public-health strategy [1].

4.2 Data and Methods

4.2.1 Surveillance and Progression-of-disease

Surveillance data

The surveillance of AIDS in Europe is co-ordinated by the European Centre for the Epidemiological Monitoring of AIDS, a WHO-EC Collaborating Centre established for this purpose in 1984. Working in close collaboration with national institutions, standardized data are collected from all countries of the European region of WHO. All 12 EC-countries were reporting by December 1985. Halfway-1991 a total of 50 673 AIDS cases had been reported in the EC (Belgium: 1.8%; Denmark: 1.6%; France: 30.7%; Germany: 13.0%; Greece: 1.0%; Ireland: 0.4%; Italy: 19.3%; Luxemburg: 0.1%; Netherlands: 3.4%; Portugal: 1.3%; Spain: 18.0%; UK: 9.4%) [161].

The data reported to the Centre relate to AIDS cases fulfilling the original or revised surveillance case-definitions of the CDC [7,8]. The 1987 revision was adopted for European surveillance purposes on January 1st 1988. Aggregate data are presented in regular Quarterly Reports and may also be consulted electronically through EURAIDS (an on-line service). The public version of the European Non-Aggregate AIDS Data Set contains individual data on more than 95 % of the reported cases. This study uses reported AIDS incidence up to June 30st 1991. Incidence is adjusted for estimated reporting delays [143] but not for under-reporting. The size of under-reporting is highly uncertain and national estimates vary between 0% and 20% [162].

Data on disease progression

Data on disease progression - the incubation period from infection (or seroconversion) to AIDS and the length of survival after AIDS diagnosis - are required to model the epidemic.

Recent evidence on the progression to AIDS in infected homosexual men indicates a median incubation period of 10-11 years and progression of approximately 25% after 7 years [163-165]. Similar findings have been reported for other risk groups [166-174]. However, there appear to be significant variations in disease progression according to age and treatment regimen. The older the individual at infection, the shorter the incubation period may be [170-173, 175-177]. Changing treatment patterns, such as the use of AZT/zidovudine before AIDS development (for example, by those with CD4-cell counts below $200 \times 10^6/l$), appear to be related to an increase in the incubation period [171,178,179].

Survival rates following the diagnosis of AIDS have been shown to depend on disease manifestation at diagnosis, age and year of diagnosis. In particular, several studies have shown significant improvements in survival among cases diagnosed in 1987 compared with those diagnosed earlier, presumably largely as a result of therapeutic intervention. Some of these studies also showed (less marked) increases since 1987. Overall median survival times among adults (including all disease manifestations and all ages) are estimated to have increased from approximately 12 months for patients diagnosed before 1987 to 18-20 months for diagnoses in 1987. [14,165,180-183]

The analysis presented below uses data on disease progression from the San Francisco City Clinic Cohort of homosexual men [165]. The observed cumulative progression rates after infection in this cohort were 51 and 54% after 10 and 11 years, respectively. Because no empirical data are available beyond 11 years, the following progression rates have been assumed: 57, 63 and 69% after 12, 14 and 16 years, respectively. Age and treatment effects are not taken into account in the present analysis. For survival time, exponential distributions are postulated. The mean survival of patients diagnosed after 1986 is assumed to be 2 years (the corresponding median being just below 18-20 months), whereas AIDS patients diagnosed earlier are assumed to have a mean survival of 1 year. However, since the observed lengthening of survival time might continue, also calculations have been included based on an increased survival time (with a mean of 3 years) for AIDS cases diagnosed in or after 1992.

4.2.2 Epidemiological Models

Statistical model for reporting delay adjustment

Several statistical estimation procedures have been developed to cope with the problem of delays in reporting AIDS cases. Here, the method by Heisterkamp *et al* is used [75,143]. Estimates of the parameters representing reporting delay are based on the AIDS surveillance data reported in successive 6-month periods and ordered according to the half-year of diagnosis. It is assumed that diagnoses arise from a Poisson process, all distributions being independent. Parameter estimation is based on maximum likelihood with goodness-of-fit measured by the deviance [184]. A software package (MIDAS) is available [185]. Because reporting patterns can change over time [186], estimates are based on more recent reports only; reports from June 1989 onwards are used. Because reporting delays show considerable between-country variation, country-specific data are adjusted before pooling to obtain adjusted AIDS incidence at the EC-level. AIDS inciden-

ce, adjusted for reporting delays, serves as input for the population-dynamic model.

Population-dynamic model

The population-dynamic model describes the spread of HIV and AIDS in a two-group population. It links a model of the spread of HIV infection with disease progression. The cumulative incidence of HIV infection in each group is assumed to follow a logistic curve. The underlying model structure and its equations have been explained in detail elsewhere [91,187]. The two groups are: (1) those with high-risk behaviour (HR; including homosexual men, intravenous drug users and heterosexuals); and (2) those with low-risk behaviour (LR; including heterosexuals, but also, for example, homosexual men with low-risk behaviour). The model is available as a software package (PC-based AIDS Scenarios).

Both groups can include individuals who are relatively less susceptible to HIV infection. A considerable proportion of the low-risk group will be such individuals. The high-risk group will include individuals whose number of partners and lack of preventive measures (high-risk activities) are offset by their specific partner networks, resulting in relatively low risk of infection. Thus, there is a maximum level for the cumulative proportion infected (saturation level) in both groups. The number of individuals who are not susceptible is the total population size minus the appropriate proportions of both risk groups (controlled for the saturation levels in the groups). A renewal rate, potentially an important parameter [188], is incorporated only for the high-risk group (details are described elsewhere [187]). Assuming a non-zero renewal rate implies the replacement of the logistic curve by a different function.

The two-group model is a first step towards modelling sub-epidemics defined by risk-related behaviour, rather than by membership of a "risk group" (a risk group may include individuals who face different levels of risk). This represents a novel approach compared with multi-group models that define risk by membership of established risk groups. An obvious advantage of the approach is that the level of risk of the resulting groups is more homogeneous. Risk depends on transmission probability, number of partners and preventive measures taken. Since it is not possible to establish the size of each group empirically, plausible combinations are obtained as a result of the search process described below. Thus the approach does not necessitate deriving the relevant information (group sizes, risk behaviour) for each of the risk groups in each EC-country. Reliable instruments and data are limited in the EC - for example, with respect to estimations of this information for the Netherlands problems to validate these estimates

occur [88].

Values for the following nine parameters have to be specified for each simulation: size of the high-risk group (sHR); saturation level in HR; renewal rate into HR (rHR); size of low-risk group (sLR); saturation level in LR; cumulative number of high-risk individuals initially infected by 1980 (HRi); cumulative number of low-risk individuals initially infected by 1980 (LRi); initial growth rate of the HIV epidemic in HR (HRw); and initial growth rate of the HIV epidemic in LR (LRw). The high- and low-risk groups together define the total population (340 million in the EC). Thus, within the model structure, only one of the two risk group sizes can be varied independently. For the specification of the number of susceptibles, sHR and its saturation level directly depend on each other. Thus there are seven independent variables.

All simulations begin in 1980. A multi-stage, systematic (but subjectively guided) heuristic approach is used to search for parameter values. In contrast to optimizing algorithms, it does not render a "best" solution, but provides several well-fitting, possible courses for the epidemic, corresponding to specific combinations of the parameter values. In the first stage, the parameter space, defined by extreme figures for all parameters that are to be varied, is systematically investigated to identify areas of possible relevance (with a good fit). Goodness-of-fit is assessed by the sum of absolute residuals expressed as a percentage of cumulative AIDS incidence. The step size by which the parameter space is traversed depends on the goodness-of-fit: it is reduced in areas where the fit seems good.

The saturation levels do not vary in this application. The saturation level in the high-risk group, which in the fitting process is directly linked to the size of the high-risk group, was assumed to be 90%; that of the low-risk group, which does not restrict the growth rate of HIV infection within our time-frame, was assumed to be 20%. Extreme figures and step sizes were thus specified for six parameters, resulting in millions of simulations.

In the second stage, possible courses for the epidemic are selected on the basis of goodness-of-fit. They are required to exhibit a sum of absolute residuals below 4% of cumulative AIDS incidence up to January 1st 1991. Within this set, simulations are compared on the basis of redundancy and heterogeneity, perhaps resulting in a description of only a few structurally different types that can "explain" the AIDS epidemic. They correspond to alternative hypotheses concerning the past course of the HIV epidemic, and so determine a set of alternative future courses of the epidemic within the model framework, resulting in alternative impact scenarios.

4.2.3 Concepts for Linkage with selected economic impact studies

Linkage with economic impact indicators

In assessing the economic impact of AIDS, case-related and general programme costs must be distinguished. Case-related costs refer to resource utilization attributed directly to the patient at a particular stage of HIV infection (for example, hospital, nursing home, district nursing care, physician consultation, family help). General programme costs refer to the provision of general services, such as public-health education, research, HIV testing and service use by the "worried-well".

Case-related costs of per person-year estimates of resource utilization and corresponding monetary amounts can be linked to the output of epidemiologic models in terms of (period-) prevalences (number of person-years during the year) [51,144,156]. Projected prevalence at the end of each year is used to derive the annual number of person-years. The accuracy of this approximation depends on the difference between the number of months lived by those who died in a given year and the number of months lived in that year by cases newly diagnosed with AIDS during that year. These could differ as a result of either increasing or decreasing incidence. (The former would result in an over- and the latter in an underestimate of the number of person-years, all other things remaining equal.) Technically, based on last year's prevalence, the highly aggregate and discrete model excludes cases who died during the year and attributes all other cases to the new AIDS prevalence. The prevalence-based approach used to project annual estimates of resource needs and costs combines (ranges for) parameter values expressing the economic impact with the projected prevalences into scenarios on economic impact (see [101,102] for an application to various health-care sectors in the Netherlands).

This paper focuses on hospital resource utilization for full-blown AIDS, since this constitutes the main part of the direct costs of the epidemic in Europe [189]. To determine capacity needs, prevalence-based projections of hospital inpatient days are expressed as the daily mean number of beds needed during the respective year. This approach uses a modification of the formula defining the occupancy rate of hospital beds [144]. Further illustrations of the method are shown using projected annual hospital costs.

Study selection

The per person-year parameter values expressing the hospital inpatient days needed and hospital costs are determined by a structured methodologic review of publications on economic impact. Several reviews summarizing and comparing the results of studies on

the resource utilization and costs of HIV/AIDS have been published [39,93,153]. Because of steadily changing treatment technologies for HIV/AIDS, it is important that cost estimates are continually updated; the update provided here is restricted to hospital resource utilization and costs in the EC-countries. Further criteria for the inclusion of studies are: (1) a clear explanation of the methodology used, allowing identification of cost components, method of data collection, and of cost estimation procedure; (2) per person-year averages given or derivable directly from the data provided; and (3) inpatient days utilization and/or costs attributable to the different stages of HIV infection [7,8,16,17].

4.3 Results

4.3.1 Existing Evidence on hospital resource utilization and costs

Application of the criteria for the selection of economic impact studies identified nine suitable studies in seven EC-countries (Table 4.1) [56,59,61,153,190-194].

The estimates in Table 4.1 are shown as costs per person-year in 1990 US dollars. Costs from the study-year's price level were converted to 1990 prices using national health-care-specific price indices. Purchasing power parities (PPP) for gross national product were used to adjust for differences in the relative unit costs of health-care services across countries [195,196]. Although these two techniques account for time-related changes in prices between studies and differences in purchasing power between countries, they do not standardize changing treatment technologies over time. This could be integrated by co-ordinated multi-centre international studies, or partial sensitivity analyses; however, neither option is pursued here.

As shown in Table 4.1, all but one [61] of the studies are small (they were based on study populations of 7.0-15.6 person-years). Only one study is relatively recent [194]; the others cover various periods between 1982 and 1988. Their size and date indicate that the basis for economic impact projections is limited - projections can only be preliminary. Furthermore, Table 4.1 shows that per person-year hospital costs for AIDS (one study gives CDC stage IV figures) vary widely. Interestingly, the studies in EC-countries with relatively low per capita gross domestic product (GDP) reported higher costs per person-year (Greece, Spain). This is in contrast to investigations based on cross-sectional data in several countries showing health-care expenditure increasing proportionally more than per

capita GDP; wealthier countries tend to spend considerably more on health care [197].

Table 4.1 *Review of studies on AIDS-related hospital costs in EC-countries: country, reference, study-period, study-size, average per person-year (ppy) inpatient days and costs*

Country	Ref	Period	Size	Ppy days	Ppy costs ¹
Belgium	[190] ²	1987-88	15.6	106	21 900
Germany	[191]	1985-86	10.0	66	13 000
	[59]	1985-87	13.0 ³	130	26 400
France	[56]	1986	⁴	⁵	22 300 ⁶
Greece	[192]	1988	< 7.0	110	70 400
Netherlands	[153] ⁷	1987-88	14.0	51	19 000
	[61]	1982-88	211.6	58	⁸
Spain	[193]	1987 ⁹	6.3	130	27 800
	[193]	1987 ¹⁰	8.5	105	25 400
UK	[194]	1989	< 12.0	⁵	28 200

¹ Costs were converted into 1990 US dollars using purchasing power parities and appropriate inflation rates (*see text*); ² Including approximately one person-year AIDS-related complex and corresponding costs; ³ Hospital inpatient and outpatient costs are based on different patient populations; ⁴ Cannot be derived, because a sample of 100 hospitalizations was examined; ⁵ Inpatient days are not reported; ⁶ Based on an assumed survival of 1.5 years after AIDS diagnosis; ⁷ Results are for CDC stage IV; ⁸ Reported figures do not allow separation of costs in AIDS and pre-AIDS stages; ⁹ Basurto region; ¹⁰ Aranzazu region.

With the exception of two outliers (US\$13 000 and 70 400), the costs are between US\$19 000 and 29 000. Estimates of the underlying utilization of inpatient days are lowest in the two Dutch studies and one of the German studies. All other studies reported over 100 days of hospital care per person-year. Several factors account for variation in amount of health-care utilization (and thus corresponding costs) between sites and countries. These include availability of services, organisation of local and national health- and social-care systems, and type and structure of treatment and care provided. The latter refers to the changing patterns of care and treatment with time: a shift from intensive care to AIDS wards, and from hospital to ambulatory care, and the changing pattern of AZT use. Follow-up of the study by Borleffs *et al.* [153] demonstrates a significantly decreasing trend in inpatient days per person-year [155,159].

Service utilization is also influenced by the patient population. The utilization rates of specific patient groups (grouped according to risk group, deceased versus alive, manifestation of AIDS) are significantly above average. The Dutch study by Borleffs *et*

al. [153] found that the costs of CDC-IV patients in the 3 months before death might be as high as US\$44 500 per person-year, because of a higher level of inpatient stays. Another Dutch study found that intravenous drug users used only 9 hospital inpatient days per person-year CDC IV, compared with 48 days by homosexual men [62,148]. Rees [194] found marginally lower costs for haemophiliac AIDS patients, and Lambert&Carrin [190] found patients with Kaposi's sarcoma to be twice as costly as *Pneumocystis carinii* pneumonia patients. However, not all studies allow an identification of the distribution of costs across these important patient classifications.

Differences in methodology of monetary cost measurement have also influenced the results in Table 4.1. To allow comparisons, the results should be presented so that the costs of care in a given country can be identified as either a higher utilization of real resources or a higher unit cost of the resources. For cost estimation and cost comparison, accurate information is required on the number of inpatient days, input in hours of medical, nursing and ancillary personnel, numbers and type of diagnostic tests, amounts of medication and unit costs of such items. The availability of such information varies for the studies included in Table 4.1.

Lambert&Carrin [190] used hospital bills, including those for outpatient hospital services, to estimate costs. Their study included personal expenditures and the costs borne by the Belgian Health Insurance Scheme; the former appeared to be up to 13% of patient's income. However, their presentation does not include a breakdown of the resource utilization, or unit costs.

Hanpft *et al.* [191] derived cost prices for physician consultations, hotel function (for example, food, linen, cleaning) and nursing from the hospital cost-accounting centre. Nursing time per AIDS patient was assumed to be 1.6 times the hospital average. Other medical services were valued by means of charges. Costs of drugs were based on purchase prices. Only resulting total costs per inpatient day were reported (US\$197 for AIDS patients). Koock-Walewski [59] used total mean costs per inpatient day of US\$173 and considered outpatient hospital costs (15% of total costs).

Hatzakis and Trichopoulos [192] used medical charges in a small retrospective study of seven patients. The costs per person-year were US\$16 900 for AZT/zidovudine and US\$53 500 for inpatient treatment and care. The Greek and Spanish studies included only AZT-treatment and inpatient costs.

Borleffs *et al.* [153] used estimated average cost-prices for an inpatient day of US\$249. This was assumed to include the salaries of an AIDS internist and a consultant nurse. Diagnostic tests, consultations (except by AIDS internists), blood-transfusions and

artificial ventilation were monetarily valued using charges, as provided by health insurance funds. Market prices were used for the costs of medication and drugs. The study included outpatient hospital costs and psychiatric hospital care.

Ginestal Gómez [193] used approximate average expenditure per bed (US\$182 in Basurto and US\$212 in Aranzazu). Estimated costs of AZT-utilization were approximately US\$3000-4000 per person-year. The studies from the UK [194] and France [56] did not consider any kind of breakdown of the costs.

Treatment patterns have been (and are) changing: the period of treatment has become significantly longer, and new (more costly) medication has been introduced (such as aerosolized pentamidine). In view of this, and the observed interstudy differences, hospital impact scenarios should be constructed for several values of the relevant economic impact parameters. Therefore, ranges have been developed for hospital costs per person-year as well as for inpatient days per person-year.

Ranges for economic parameters to investigate the impact on hospitals (bed needs, annual costs) were created by weighting the averages shown in Table 4.1. The weights used were the study size in person-years and the cumulative number of AIDS cases up to June 30st 1991 in the respective country (*see* Table 4.1). The first takes into account that a result based on a large study is more valuable (more representative of the country concerned) than a result from a small study (the sizes of the studies from Greece and the UK are assumed to be 3.5 and 6 person-years, respectively). The second accounts for the relative importance of the AIDS epidemic in a country, compared with the EC as a whole. This relative importance is assumed to be constant (future changes in the distribution of AIDS cases between EC-countries are not considered). The upper and lower bounds of the range are defined by expanding the symmetric interval around the weighted average to the point where all reported study results, except some extreme values (130 inpatient days; costs of US\$13 000 and US\$70 400), are included.

Projections of hospital bed needs are based on the weighted average of 80 inpatient days per person-year, with lower and upper range values of 50 and 110 days, respectively. The weighted average of US\$23 300 per person-year is used for projections of annual hospital costs. The range around the average is US\$18 400-28 200.

4.3.2 EC-scenarios

The methods described, together with the available information on hospital costs for full-blown AIDS patients, were used to design scenarios for the EC. The parameters of the simulation model were tuned to the annual AIDS-incidence between 1981 and 1990 as reported by June 30st 1991 [198] and adjusted for reporting delays (Fig 4.1).

Fig 4.1 *AIDS incidence in the European Community by 6-month period (i: January-June; ii: July-December), as reported up to June 30st 1991 and as expected after adjustment for reporting delays (white: reported; black: expected)*

Several hundreds simulations showed a goodness-of-fit below 4%. All involved a similar basic type of subepidemic: an extremely fast infection in a small high-risk group, in which the major proportion of susceptibles had been infected for at least 2 years. They appeared to fall into four groups, differing in two important and sensitive coefficients: (1) the initial growth rate of the HIV epidemic in the low-risk population (LRw); and (2) the renewal rate of the high-risk group (rHR). Four typical and well-fitting simulations (one from each group) were selected for further analysis (Table 4.2). To optimally reflect the effects of the essential differences, the parameters HRi, HRw and LRi were set to the same values in each of the four simulations, although small changes would (slightly) improve the goodness-of-fit. Typically, a non-zero rHR has to be accompanied by a slightly smaller sHR to attain the desired level of goodness-of-fit.

Table 4.2 *Parameter values in the population-dynamic model of the four simulations selected*

	sHR	HRi	HRw	rHR	sLR	LRI	LRw	Goodness of fit
A	230	4.1	240	0	340	100	10	2.5
B	215	4.1	240	5	340	100	10	3.5
C	230	4.1	240	0	340	100	60	2.6
D	215	4.1	240	5	340	100	60	3.7

sHR: size of high-risk group in thousands (saturation level: 90%); HRi: number (thousands) with high-risk behaviour infected by 1980; HRw: initial growth rate of the HIV epidemic in HR in % per annum; rHR: maximum annual renewal rate in HR in % per annum; sLR: size of low-risk group in millions (saturation level: 20%); LRI: number with low-risk behaviour infected by 1980; LRw: initial growth rate of the HIV epidemic in LR in % per annum; Goodness-of-fit: sum of absolute residuals expressed as percentage of cumulative AIDS incidence (up to January 1st 1991).

The types of epidemic described all feature a very high initial annual growth rate in the cumulative number of HIV infections, which later declines rapidly to a minimum (scenarios A and C) or to a long-term steady-state growth (for models with renewal of the high-risk group - scenarios B and D). (Fig 4.2)

Given the development of AIDS incidence in the EC, and the two-group approach, it was not possible to identify any narrow ranges for the initial growth rate of HIV infections in the low-risk population. Accordingly, two alternatives are presented: an "optimistic" simulation with a relatively low growth rate (which could be even smaller), and a "pessimistic" simulation with a relatively high growth rate (which could be even higher). Thus the type of epidemic hypothesized is that of a "flash" of infection in a small group of individuals with high-risk behaviour, together with a quite different (and so far unknown) secondary epidemic in the low-risk group.

The best-fitting models had no renewal rate for the high-risk group, and so support the "flash" hypothesis, although the assumption of stability of membership of the high-risk group for over 10 years appears somewhat implausible. Hence, two less well-fitting simulations with small renewal rates have also been included.

Fig 4.2

Growth rate of cumulative incidence of HIV infections (logarithmic scale) in four scenarios - scenario A (triangles top-up): low rate of infection in low-risk group (LR), no renewal in high-risk group (HR); scenario B (circles): low rate of infection in LR, with renewal in HR; scenario C (boxes): high rate of infection in LR, no renewal in HR; scenario D (triangles top-down): high rate of infection in LR, with renewal in HR (see Table 4.2 for specification of scenarios)

Fig 4.3

Estimated annual incidence of HIV infections: reconstruction (1980-1990) and projection (1991-2000) according to four scenarios - scenario A (triangles top-up): low rate of infection in low-risk group (LR), no renewal in high-risk group (HR); scenario B (circles): low rate of infection in LR, with renewal in HR; scenario C (boxes): high rate of infection in LR, no renewal in HR; scenario D (triangles top-down): high rate of infection in LR, with renewal in HR (see Table 4.2 for specification of scenarios)

Two types of future spread can be clearly differentiated by the rate of infections in the low-risk group, rather than by the renewal rate in the high-risk group (Fig 4.3). All four scenarios show a peak in HIV incidence around 1984 (range for annual number of cases: 57 300-59 600). The modelled cumulative HIV incidence on December 31st 1988 was 207 000-234 000, which is rather low compared with a recent report of approximately 400 000 (using backcalculation) [199]. However, the latter estimates were for AIDS incidences that had been inflated for under-reporting (10%) and adapted for revisions in the AIDS case-definition. An important implication of the "flash" hypothesis developed within the present model is that the main groups currently at risk, and thus the potential targets of preventive action, may not be well identified, while the "old" and recognized dangers could now have a relatively less important role. Compared with HIV infection, the corresponding AIDS incidence curves display a smaller but still significant variance between the hypotheses (Fig 4.4). A peak in AIDS incidence following that in HIV incidence is projected around 1992 (range for annual number of cases: 15 500-17 300).

Fig 4.4

Annual AIDS incidence: fitted values (1980-1990) and projections (1991-2000) according to four scenarios - scenario A (triangles top-up): low rate of infection in low-risk group (LR), no renewal in high-risk group (HR); scenario B (circles): low rate of infection in LR, with renewal in HR; scenario C (boxes): high rate of infection in LR, no renewal in HR; scenario D (triangles top-down): high rate of infection in LR, with renewal in HR (see Table 4.2 for specification of scenarios)

Impact assessment is based on prevalence figures. Simulations with the lowest and the highest future AIDS prevalence (scenarios A and D) have been used for the presentation of the future impact of full-blown AIDS. Because of the high uncertainty about future AIDS incidence and prevalence (future modelling of which may have to account for significant effects of changes in medical technology and inclusion of new population groups), impact scenarios are restricted to the medium term only (1995).

For comparative purposes, the impact assessment also includes the year 1990 as baseline (scenarios A through D have approximately the same prevalence at the end of 1990 of 20 800 AIDS cases). Survival times of persons with full-blown AIDS will also affect the future need for hospital care and corresponding costs. A current mean of 2 years is assumed and unchanged in scenarios A and D; however, given current and future improvements in AIDS treatment, an increase to 3 years for AIDS cases diagnosed from 1992 onwards is also considered (A* and D*). Resource utilization (and costs, *see below*) per person-year are assumed to be the same for both survival distributions. Therefore, a lengthening of survival is accompanied by a proportional increase in resource utilization and costs during the whole AIDS stage. 1995 AIDS prevalence figures in A, A*, D and D* are 21 800, 28 200, 29 300 and 37 300 cases, respectively.

An 85% occupancy rate has been assumed for hospital beds (*see* [200] for a similar analysis for Germany). Assuming 80 hospital inpatient days per person-year, scenario D* indicates a need for 9600 hospital beds in 1995 (Fig 4.5). All scenarios are above the 1990 level of 5400 beds. The use of the broad range of inpatient days per person-year accounts for most of the variation in the 1995 projections. Lengthening survival increases bed needs by approximately 28% (in both scenarios A and D), whereas differences in the epidemiological course of HIV infection produce a variation of approximately 33% (both between A and D and between A* and D*).

Analogous hospital cost projections for care and treatment of full-blown AIDS patients are shown (Fig 4.6). Projected costs are based on constant (1990) prices and constant PPP. Assuming an average cost of US\$ 23 330 per person-year the high annual cost projection of scenario D* is US\$ 870 million in 1995 (compared with the 1990 baseline estimate of US\$ 485 million), whereas the lowest projection for 1995 in scenario A is US\$ 510 million. The use of the range around the average for the hospital costs per person-year (US\$ 18 400-28 200) extends the range for annual hospital costs in the EC to US\$ 400-1050 million.

Fig 4.5

Prevalence-based estimates of hospital bed needs in 1995 in two variants of scenarios A and D (A, D: mean survival of 2 years; A*, D*: mean survival of 3 years) for a range of inpatient days per person-year AIDS, compared to 1990 as baseline - scenarios A, A*: low rate of infection in low-risk group (LR), no renewal in high-risk group (HR); scenarios D, D*: high rate of infection in LR, with renewal in HR (see Table 4.2 for specification of scenarios)

Fig 4.6

Prevalence-based estimates of annual hospital costs in 1995 in two variants of scenarios A and D (A, D: mean survival of 2 years; A*, D*: mean survival of 3 years) for a range of hospital costs per person-year AIDS, compared to 1990 as baseline - scenarios A, A*: low rate of infection in low-risk group (LR), no renewal in high-risk group (HR); scenarios D, D*: high rate of infection in LR, with renewal in HR (see Table 4.2 for specification of scenarios)

4.4 Discussion

4.4.1 Scenario Results

In this paper methods have been developed to assess the economic impact of HIV infection and its related diseases. A population-dynamic simulation model of the epidemic has been used to obtain projections for two important impact indicators - hospital bed needs and costs - for the EC-countries. Because information on the rate of infection, disease development and needs and costs of care and treatment remains incomplete, the resulting projections are preliminary. However, this is inherent to addressing the impact of a rapidly evolving health problem, in contrast to many economic impact studies in the health-care field directed at more-or-less steady-state situations.

The application of a statistical procedure has allowed to make appropriate corrections to reported AIDS incidence to account for delays in reporting AIDS cases. A population-dynamic simulation model has been used to attribute the resulting (adjusted) AIDS incidence to alternative types of underlying HIV epidemic. One such epidemic in the high-risk group appears to be consistent with the data: an extremely rapid infection of a small high-risk group, with the majority of susceptible individuals having been infected for more than two years (the "flash" of infection hypothesis). Two extremes of the possible types of spread, consistent with the data, are presented for the low-risk population. One is based on an "optimistic" simulation of the epidemic with a relatively low infection rate; the other on a "pessimistic" simulation with a relatively high infection rate. An important implication of the "flash" hypothesis is that the main groups currently at risk, and thus the potential targets of preventive action, are not well identified, while the known dangers may now be playing a relatively less important role (although probably continuing to exist). For both types, one simulation with and one without renewal in the high-risk group were selected for impact assessment. Compared to another recent estimate of 400 000 [199], the four resulting scenarios indicate a rather low cumulative HIV incidence in EC-countries (of 207 000-234 000 as of December 31st 1988) and all project a peak in AIDS incidence around 1992 of 15 500-17 300 cases per year. Of course, these ranges depend strongly on the assumption of the "flash" of infection and on uncertainty about the follow-up epidemic.

It has been shown that, without a change in the needs of inpatient days per person-year, even in the most optimistic epidemiological simulation, hospital bed needs for full-blown AIDS in the EC in 1995 will be above the estimated level for 1990. If 80 inpatient

days per person-year are assumed for 1995, the most pessimistic epidemiological simulation projects a maximum of 9600 beds needed for that year, which on the basis of current estimates could represent 0.45% of the total number of hospital beds available in the EC [196].

The hospital cost projections for full-blown AIDS in 1995 range from US\$400 million to 1050 million. Cost of hospital treatment and care for AIDS patients by 1995 may at best be similar to that today (approximately 0.15% of health-care expenditure of all EC-countries). This percentage could be as high as 0.30% if the upper bound of the range applies. It should be noted that the availability of health-care-specific PPP expressed in ECUs would improve this type of EC-directed studies [196,201,202].

Hospital costs for HIV/AIDS constitute an estimated 86% of the direct patient-related costs in the Netherlands [101]. Furthermore, the estimates of hospital resource utilization and corresponding costs presented here are all minimum estimates, in that hospital bed needs and costs of patients in pre-AIDS stages are not included. Leidl *et al.* [144] discuss the impact of their inclusion.

It is important to note that the assumptions of a constant incubation period distribution and a constant or even increasing survival time could be inaccurate. Although early treatment with AZT/zidovudine will lengthen progression to AIDS, it may shorten survival time after developing AIDS [203]. The use of antiretroviral drugs in combination with prophylaxis (for example, for *Pneumocystis carinii* pneumonia) appears to be an important intervention in the AIDS-free stage, also prolonging the incubation period. This may increase costs in the AIDS-free period, and perhaps decrease the per person-year parameter values for inpatient days and costs in the AIDS stage. It is not yet possible to predict the effect of these influences on impact scenarios. Investigations of these developments have either indicated cost savings [126,204], or changing patterns of spread of HIV, possibly increasing the AIDS-related death rate [92,205].

HIV/AIDS-modelling is still developing. Future work might include mathematical modelling using differential equations and/or an extension of the two-group structure to more than two groups. Possible links between the groups should also be studied [88]. Several model types, requiring different types of information, have been developed for HIV/AIDS [141,142,206]. These data needs, which have been specified by modellers and are well-known in the literature, include estimates of infectiousness and transmission probabilities, incubation time distribution, trends in HIV incidence/prevalence (within risk groups and regions), occurrence of risk behaviour (sexual, drug use) and effectiveness of prevention and treatment [207].

4.4.2 Data Requirements for Scenario Analysis

Cost data from existing studies can be used to produce preliminary and illustrative projections of AIDS impact on hospitals. However, standardization of these estimates must be improved if they are to be more valuable for the specification of impact parameters in scenario analysis. The main objective of standardization is to separate the influence of methodological factors (for example, concepts and procedures) causing variations in cost estimates, and to devise a protocol to standardize methodology, such that actual variation in resource utilization and costs can be more clearly identified. Retrospective adjustment of results is likely to be difficult and time-consuming, and may allow only small improvements in comparability.

The methodological aspects of standardization of cost studies discussed here are restricted to patient-related costs of HIV/AIDS. Prevention (for example, screening of blood donations), AIDS education and information and research are excluded; as are indirect costs (such as loss of productive capacity) associated with life-years lost and absence from work; and reduction in quality-of-life. Preliminary work on a standardized cost framework has involved the identification of sets of guidelines in several areas for which standards can most profitably be applied [66]:

- (1) a standardized approach to health-care utilization data collection;
- (2) standard principles for estimating the unit costs of service use; and
- (3) use of a standard format for the presentation of results.

For (1), the basic methodological requirement is that information on service use must be recorded or available on an individual (patient) basis. Prospective data collection is generally preferred to retrospective collection, mainly because the latter soon tends to produce inaccurate reflection of the present resource utilization and costs (due to rapidly altering treatment patterns). Prospective data collection also allows inclusion of all relevant parameters, giving rise to fewer data interpretation difficulties and errors. However, it is relatively time-consuming and expensive.

For (2), cost estimates involve multiplying the physical quantities of resources used to provide HIV/AIDS-related treatment and care (for example, staff hours, inpatient days, medication) by a price for each unit of resource input. Prices should reflect the true opportunity cost (the value of the best alternative use of the resources, assessment of which will depend on local circumstances) as closely as possible. If possible, current market prices of different resource inputs should be used (for example, hospital-staff time spent on treatment and care should be valued using hourly payment rates, and daily

medication administered should be valued at the current commercial prices). Hospital charges are likely to be highly unrepresentative of opportunity costs and should not generally be used. The method used for apportioning overhead, administration, training and hotel costs should be made explicit. If costs are not based on direct accounting, a precise description of the *ad hoc* procedure of estimation should be provided. Information availability and accounting procedures are likely to be heterogeneous among countries and even among institutions in a country. Principles in this area should therefore represent generic recommendations rather than strict operational procedures or criteria for computing costs.

Several dimensions should be considered for (3). Per person-year estimates should be available for annual budget planning, and lifetime cost estimates are required for mapping trends in average costs over the course of HIV infection and AIDS. It is important that definitions and classifications of disease stages, risk groups and other variables relevant for categorizing individuals are agreed upon. Presentation should explicitly include the period of data collection, the number of person-years of observation and the number of individuals surveyed.

One concludes that uncertainty about available evidence on resource utilization and costs in Europe (due to differences in data collection and cost-estimation methods) is an important source of variation when deriving parameters of economic impact functions. Although a considerable number of cost studies have been conducted, they have produced few data of use in developing impact functions over time. More (prospective) longitudinal empirical work is required. Furthermore, these studies did not use a standard approach, hindering their comparison and integration. This problem has also been recognised in economic investigations of treatment and care for other diseases [208]. It is therefore proposed that guidelines be provided for estimation of HIV/AIDS-related personal health-care costs, allowing valid comparisons between studies performed at different times and settings and by different researchers.

The discussion in this paper represents a starting point for systematic inter- and intranational estimation and comparison of HIV/AIDS resource utilization and costs. The principles of cost standardization should be developed and extended. On a practical level, difficulties in data collection and limited research resources mean that, for studies to be comparable, the initial application of a standardized cost framework is likely to be restricted to hospital treatment and care for people with symptoms of HIV infection. The further away one moves from strict hospital costs, the more uncertain and unreliable data become [134,209]. Inclusion of data on resource utilization and costs in pre-AIDS stages

allows analyses on the impacts of treatment interventions on a large scale, particularly in the early stages of the disease. A longer-term objective would be to extend the standardized framework to measurement of resource utilization and costs outside the hospital (i.e., community and social care) and to other major diseases. The combination of estimates produced within a standardized cost framework and epidemiological data would produce higher quality scenarios on current and future aggregate resource utilization and costs in the health- and/or social-care sectors of individual European countries or regions such as the EC. This would allow more valid multi-national comparisons of the total cost of AIDS in a country (in absolute terms) and as a proportion of health-care budgets.

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Chapter 5

AIDS Scenarios for the Netherlands; the economic impact on hospitals

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Abstract

Objective To assess the financial-economic impact of HIV/AIDS on the health-care system in the Netherlands.

Data & Methods Two types of data are used: (1) routine surveillance-data on AIDS incidence; and (2) information on inpatient and outpatient hospital resource utilization and corresponding monetary costs. Progression-of-disease is modelled using a multi-stage model, with stages corresponding to clinical classifications and different phases of health-care need. Economic impact is analyzed for all stages in three scenarios: a reference and two alternative scenarios.

Results By the end of the century hospital annual bed needs would reach 220 beds if yearly new HIV infections in the 1990s remain at the level estimated for the end of the 1980s, and if the intensity of hospital care remains constant. Minimum needs of 125 is projected if no new HIV infections occur in the 1990s. Hospital costs in 1993 are estimated to amount 33.8 million ECUs. Scenarios indicate a range of 26.7-50.7 million ECUs for annual hospital costs by the end of the century (price level: 1993). The proportion of the costs for hospital inpatient care and cure in total hospital costs increases.

Conclusions Projected hospital bed needs of 125-220 for HIV/AIDS by the end of the century is limited compared to the projections for coronary heart disease and stroke, but approaches that for lungcancer, pneumonia and diabetes. Hospital costs are estimated to have been 85% of total health-care costs for HIV/AIDS in 1993. In 1993, the estimated proportions in hospital costs are 41% for inpatient care, 20% for inpatient cure and 39% for outpatient facilities. Scenarios indicate a decreasing share of outpatient costs - possibly down to 30% of total hospital costs for HIV/AIDS by the end of the century - illustrating the growing relative importance of the inpatient-care-intensive full-blown AIDS stage for the hospital costs. Annual hospital costs for HIV/AIDS by the end of the century are projected to reach up to 0.53% of extrapolated hospital costs for all diseases. A present value of 38 million ECUs (23%) of hospital costs projected in the reference scenario might be avoidable, during the period 1994-2000. However, with unchanged treatment patterns a present value of 127 million ECUs for hospital costs during the same period is projected to represent unavoidable costs (discount rate: 5%). In the Netherlands, data needs in the field of economic impact assessment of HIV/AIDS especially refer to registrations of non-hospital outpatient resource utilization and costs.

5.1 Introduction

In 1992 the Dutch AIDS Scenario Study, conducted within the framework of a WHO-initiative, was concluded [100,101]. The study describes the epidemiological, socio-cultural and economic impact of AIDS in the Netherlands during the first decade of the epidemic (1980-1990). Scenario analysis is used to project the impact of AIDS up to the year 2000. This paper presents an update of this analysis focusing on financial-economic aspects. Projections by means of similar methods have been published in the literature for the US [48,52,210], the UK [211], Catalonia [212], Spain [213], Portugal [214] and Germany [200].

The importance of studying the economic impact of disease has been emphasized by the EC [1]. In the case of AIDS the importance is strengthened since the epidemic is ongoing and effective control measures have been [215] and are still scarce. Results on impact assessment are valuable for planning disease-specific services and allocating resources over health-care sectors and diseases. One way of analyzing economic impact is by scenario analysis linking patient-based information on resource utilization and monetary costs with epidemiological modelling. These aspects have been discussed previously [216]. Other work has examined the needs and limitations of scenario analysis for linking a range of impact indicators with epidemiological modelling [160]. This research builds on results from two activities of the EC: the Concerted Action on Statistical Analysis and Mathematical Modeling of AIDS [108,141,217] and the Study on Economic Aspects of AIDS and HIV Infection [109]. Also some WHO activities have addressed the same problems [39,154]. In the Biomedical and Health Research Programme (1990-1994; BIOMED I) of the EC the field of research will be developed further in the Concerted Action on Multi-national AIDS Scenario Analysis [107]. Recently, preliminary scenarios on hospital bed needs and costs for EC-countries have been published [144,218].

This paper focuses on: (1) an updated application of epidemiological modelling using recent surveillance data; (2) an extension of the epidemiologic model to better distinguish disease stages according to different health-care needs; (3) the linking of epidemiological developments with recent data on hospital inpatient-days utilization and corresponding costs; and (4) scenario results on hospital resource utilization and monetary costs up to the year 2000.

5.2 Data

5.2.1 Epidemiologic Data

Surveillance

The surveillance of AIDS in The Netherlands is undertaken by the GHI in Rijswijk. The surveillance case-definition of 1987 is applied [7,8]. Reporting of AIDS diagnoses is on a voluntary basis, and usually takes place within several months post-diagnosis, but in exceptional cases can be over two years. The annual number of diagnoses are adjusted for this reporting delay [143], using the GHI report as of June 30st 1993 [219]. This analysis is done separately for the main patient groups of homosexual men, intravenous drug users, heterosexuals and others. The former three groups make up 95 % of the cumulative reported diagnoses. The majority of the rest of reported diagnoses are recipients of blood and blood products.

Progression-of-disease

Data on disease progression - the incubation period and survival after AIDS diagnosis - are required to model the epidemic. Based on an analysis from the European Centre for the Epidemiological Monitoring of AIDS (Paris), an overview of both aspects has recently been presented [218]. The analysis presented below uses an incubation period closely resembling that observed in the San Francisco City Clinic Cohort of homosexual men [12]. Variability in incubation period due to age and patient group are not taken into account in the present analysis. For AIDS-stage survival Dutch data are used: median survival was found to have risen from 12 months for patients diagnosed before 1987 to 20 months for patients diagnosed in 1987 [14]. Since it is unknown whether survival will remain constant or keeps increasing both possibilities are incorporated into the scenarios.

5.2.2 Economic Data

Information on hospital resource utilization and corresponding monetary costs is derived from a database at the University Hospital Utrecht (Academisch Ziekenhuis Utrecht; AZU). This registration system has been developed by AZU in co-operation with RIVM. The design of this system has been described previously [151] and analyses of the data for the period January 1987-June 1990 have been published [220].

Resource utilization is influenced by patient-population characteristics such as

disease stage and patient group [62]. Table 5.1 shows, for different disease stages and patient groups, the number of hospital inpatient-days per observation-year (poy) during January 1988-December 1991². Patient data for 1987 are not considered, since they are assumed not to reflect the current inpatient-day utilization. In the early period of HIV/AIDS treatment, poy hospital inpatient days were significantly higher than later in later years [220]. It is likely that specialists experience of treating the first wave of HIV/AIDS patients led to an improved management of care for later patients [221].

Table 5.1 *Inpatient days per observation-year and number of observation-years (between parentheses) by CDC stage and patient group*

	Homosexual men*	Drug users	Heterosexuals	Total
CDC II/III	1.7 (136.3)	0.2 (17.4)	1.1 (26.5)	1.5 (180.2)
CDC IV	28.7 (108.2)	29.3 (3.2)	31.3 (5.0)	28.9(116.4)
Early-CDC-IV	24.7 (48.5)	..	..	24.8 (50.6)
Late-CDC-IV	101.2 (14.3)	..	..	93.8 (17.1)

CDC stages II and III are combined (CDC II/III). For CDC IV separate figures for the final half year before death (*late-CDC-IV*) and the remaining part of the stage (*early-CDC-IV*) are presented (see text).

* Including homosexual intravenous drug users; .. Number of observation-years insufficient for reliable estimation.

Source: AZU/RIVM-registration system.

In Table 5.1 disease stages are classified according to the CDC definition [16,17], with CDC stages II and III combined (CDC II/III). In the CDC-IV stage, higher poy utilization rates are reported for patients who have died compared to those alive, due to a higher inpatient-stay frequency [153]. Therefore, CDC-IV stage is divided into two phases:

- 1 the final half year in CDC IV preceding death³ (*late-CDC-IV*); and
- 2 the whole CDC-IV stage excluding that final half year for deceased patients and excluding the second half year of 1991 for patients alive by the end of 1991

² The observation-year concept is used to take into account that some patients enter the registration system during a year, whereas others leave during a year. One observation-year corresponds to one patient being in contact with the hospital for a whole year, or with two patients both in contact with the hospital for a half year, etcetera. Dividing the total number of registered inpatient days by the number of observation-years results in poy inpatient days.

³ In case the period between CDC-IV diagnosis and death lasted less than a half year the whole CDC-IV stage is used.

(*early*-CDC-IV).

Finally, inpatient-day utilization differences according to the three main patient groups are examined in the Table.

As yet, insufficient observation-years are available to be able to identify statistically significant differences between patient groups in *early*-CDC-IV and *late*-CDC-IV. One striking finding is the low inpatient-day utilization of intravenous drug users in the CDC-II/III stage. This finding contrasts with results assessed in an Amsterdam hospital, where intravenous drug users were found to have a higher inpatient-day utilization than homosexual men in the CDC-II stage [62]. For the scenarios patient-group-specific figures are not yet used, until more reliable data are available.

Monetary cost estimates used in the scenarios are direct medical costs. The cost per inpatient day for the period January 1988-December 1991 is estimated at 310 ECUs for CDC-IV-stage patients and 210 ECUs for CDC-II/III-stage patients⁴. The higher costs for the former reflect the greater intensity of care they receive. Based on estimated cost prices and pharmacist prices [58], these hospital inpatient-care costs include "hotel costs", costs of nursing, use of disposables and general drugs. However, they exclude treatment (for example, artificial ventilation, blood transfusion), consultations (for example, internist, AIDS nurse), diagnostic procedures (for example, blood-cell counts) and AIDS-specific drugs (for example, AZT/zidovudine, acyclovir and ddi). These costs are defined as the costs of hospital inpatient cure. A third set of costs are those of hospital outpatient facilities.

Since no recent figures for the costs of inpatient cure and outpatient facilities are yet available the ratio of poy estimates for inpatient-cure costs, outpatient costs and inpatient-care costs as reported earlier for 1987-1988 is applied [153]⁵. For the whole CDC-IV stage, poy inpatient-care costs, inpatient cure costs and outpatient costs constitute, respectively 53, 26 and 21 % of total hospital costs. For the CDC-II/III stage the respective percentages are 9, 7 and 84 %. As poy hospital inpatient-care costs for CDC-IV have decreased by almost 25 %, a similar decrease is assumed for both inpatient-cure and outpatient hospital costs. Further, for the costs of cure in both the *early*-CDC-IV and the *late*-CDC-IV phases a proportional relationship with respect to inpatient days is

⁴ Amounts are expressed in 1993 prices. To transform the original cost figures - expressed in 1988 Dutch guilders (*f*) - the nominal growth (factor: 1.21) of Dutch health care costs during 1988-1993 is used [222]. For the exchange of *f* into ECUs the exchange rate of September 7th 1993 is used (1 ECU equals *f*2.12).

⁵ In the discussion section sensitivity analysis is performed with respect to this assumption.

assumed. For outpatient costs an inversely proportional relationship in these two phases is assumed, demonstrating that outpatient costs will be relatively low during periods with high inpatient-day utilization. Both assumptions are in line with previous findings⁶. Inpatient-cure and outpatient costs are based on tariffs and pharmacist prices. The poy cost estimates are presented in Table 5.2.

Table 5.2 *Assumptions on hospital costs (in 1993 ECUs) per observation-year by CDC-stage*

Hospital inpatient care	CDC-IV	8940 (7734, 29 079)
	CDC-II/III	312
Hospital inpatient cure	CDC-IV	4381 (3776, 14 199)
	CDC-II/III	214
Hospital outpatient	CDC-IV	3487 (4045, 1076)
	CDC-II/III	2778

CDC stages II and III are combined (CDC II/III). The figures for CDC IV corresponding to *early-CDC-IV* and *late-CDC-IV*, respectively (*see text*) are presented in parentheses.
Source: AZU/RIVM-registration system.

5.3 Methods

5.3.1 Introduction

The AIDS-impact model links an epidemiological progression-of-disease submodel with a submodel for hospital inpatient-day needs and costs. The model has been used in the Dutch AIDS Scenario Study conducted by RIVM and the Netherlands Institute for Mental Health, commissioned by the STG. The present model represents an extension of this work enabling us to take the effects of early treatment into account. In recent years treatment with antiretroviral drugs (AZT/zidovudine) in combination with prophylaxes (for example, for *Pneumocystis carinii* pneumonia) has become widely used in the asymptomatic pre-AIDS stage, affecting the epidemiology of AIDS as well as health-care resource utilization. Adherence to early treatment is assumed to cause an extension of the

⁶ Borleffs *et al.* [153] assessed that for patients in the last three months of CDC-IV before death poy hospital inpatient-care costs, hospital inpatient-cure costs and hospital outpatient costs were, respectively US\$23 800, US\$10 500 and US\$1800. Excluding these final three months of deceased patients the amounts were, respectively US\$8800, US\$4400 and US\$4400. The more than halving of inpatient-care and inpatient-cure costs is accompanied by more than a doubling of outpatient costs.

incubation period of, on average, one year⁷.

Fig 5.1

Diagram reflecting the model for progression of disease: five stages (acute infection, unknown asymptomatic infection, known asymptomatic infection, symptomatic pre-AIDS disease and AIDS), the fraction of HIV-infected persons adhering to early treatment (f) and mean durations of stay (within the boxes)

5.3.2 Epidemiologic Modelling

Progression-of-disease submodel

The progression-of-disease submodel has two characteristics: a compartmental structure with the duration-of-stay in each compartment exponentially distributed (Fig 5.1). The compartmental structure differentiates between the five relevant stages for health-care need, also corresponding to clinical classifications. The first stage represents acute infection. The asymptomatic phase of HIV infection is represented by two stages (unknown - and known asymptomatic). The former comprises persons unaware that they are seropositive. Known asymptomatic is the stage when the infected persons have learned about their serostatus. In this stage a person becomes eligible for early treatment and is assumed to be under observation in a hospital. Adherence to early treatment prolongs the duration of stay in this stage by one year on average. Therefore the stage of known asymptomatic is illustrated by two equivalent boxes (fraction f adheres to early treatment,

⁷ This assumption could be challenged, though. Some recent studies indicate that the effect of AZT/zidovudine is rather limited or even absent at all [223,224].

fraction $(1-f)$ does not)⁸. Finally, the symptomatic pre-AIDS stage, and the final stage of AIDS are included. Persons in these two stages are assumed to be aware of their seropositivity. The combined stages of known asymptomatic and symptomatic pre-AIDS are referred to as the phase of known seropositive.

Reasonable values for the mean durations of stay in the five stages are, respectively 1, 4, 5 (6 in case of early treatment), 1 and 3 years (also reflected in Fig 5.1). The resulting incubation period excluding early treatment (*see* Fig 5.1; $f=0$) has a median of 9.6 years and mean of 11 years. This median survival time in the AIDS stage is slightly above results for 1987 of the Dutch AIDS survival study, mentioned above. Also, the lengths of the acute infection, asymptomatic and symptomatic pre-AIDS stages are conform to the notions that one has about them. Pragmatically, it is assumed that on average an HIV-infected person becomes aware of seropositivity, halfway through the asymptomatic pre-AIDS stage (including acute infection and excluding early treatment).

Backcalculating and projecting incidence and prevalence

The progression-of-disease submodel comes into the modeling process twice: it is central in the backcalculation procedure for estimating past HIV incidence and is necessary to make projections (1993-2000) of the future epidemic (and connected hospital inpatient-day needs and costs). The estimated past HIV incidence (infection curve) is assessed backcalculating on the basis of the AIDS incidence⁹ [20,80,83,225]. Since the attack rate of AIDS is low in the first years after infection the AIDS incidence provides little reliable information to estimate HIV incidence in the most recent years. Therefore estimates of the infection curve are confined to the period up to 1990 only. In addition, a more stable infection curve is achieved by aggregating the attack rates in the first three and a half

⁸ In this paper for simplicity assume $f=1$ is assumed, from 1990 onwards, and $f=0$ in previous years. This corresponds to a full coverage of the infected population since 1990 (which certainly is an overestimate).

⁹ The backcalculation procedure is as follows:

$$A(t) = \sum_{s=0}^t P(s) * I(t-s)$$

where $A(t)$ is the AIDS incidence in year t ; $P(s)$ equals the probability of developing AIDS in the s th year after the year in which infection took place; $I(t)$ equals the HIV incidence in year t . For $A(t)$ the AIDS incidence 1982-1992 as registered by June 30st 1993 and adjusted for reporting delays is used, $I(t)$ is established by iterative calculus. In our model $A(t)$ occurs over the duration of the year, whereas $I(t)$ is assumed occurring at the mid-point of the year. These assumptions enable to accurately calculate the relevant quantiles of the incubation period distribution.

years and relating this total to the period between two and a half years and three and a half years. Thus, implicitly the start of the epidemic of HIV infections is assumed three years before the start of the AIDS epidemic (1979 and 1982, respectively). Further, it is assumed that 90% of the HIV-infected persons will have developed AIDS after 20 years; in the long run, theoretically, this even approaches 100%. Possible mortality in pre-AIDS stages and persons who will never develop AIDS (possibly due to immunological or virological reasons) are not included. Apart from a British study which suggests a possible relevant effect there is no empirical evidence to assess the extent of pre-AIDS mortality [226]. Even if it occurred, evidence of HIV-infected persons not going to develop AIDS would not be available until the late 1990s at the earliest.

In the next step the progression-of-disease submodel is used together with the infection-curve for projecting the HIV/AIDS epidemic for 1993-2000 within three variants. In the first two variants - R(eference) and T(herapy) - the infection curve for 1990-2000 is projected to equal the average level of the estimated three most recent HIV incidences (1987-1989)¹⁰. Variant R serves as the point of reference, assuming a constant distribution of survival in the AIDS stage. In variant T, new AIDS therapy causes a lengthening of survival in the AIDS stage from 3 years on average to 4 years (starting in 1992). The third variant S assumes no new infections in 1990-2000. This variant basically constitutes a subvariant of the other two representing the "unavoidable part of the epidemic". In variant S no lengthening of survival is assumed. In-migration of estimated and assumed HIV incidence, progression-of-disease and out-migration due to AIDS deaths determine the prevalences in each stage.

5.3.3 AIDS-impact Model

The final component of the AIDS-impact model links the output of the epidemiological submodel with a framework defining hospital inpatient-day needs and costs per person-year (ppy), for each disease stage¹¹.

Observed hospital inpatient-day utilization per observation-year (poy) and estimated poy monetary costs of inpatient care, inpatient cure and outpatient facilities are

¹⁰ An analogous assumption is used by Brookmeyer and Liao [210] to assess future health care costs due to HIV/AIDS in the US.

¹¹ One person-year in a particular disease stage corresponds to one person being in the stage for a whole year, or to two persons both in the stage during a half year, etcetera.

used as proxies for ppy hospital inpatient-day needs and ppy monetary costs of hospital inpatient-care, inpatient-cure and outpatient resource needs (Tables 5.1 and 5.2). Utilization figures of CDC-IV and CDC-II/III disease stages are assumed for needs of AIDS and known seropositive patients, respectively^{12,13}. Ppy needs and costs are assumed constant during the seropositive stages, whilst separate estimates for ppy *early*-CDC-IV and ppy *late*-CDC-IV utilization and corresponding costs are used to reflect ppy resource needs and costs in the AIDS stage¹⁴.

Scenarios of hospital resource needs and corresponding costs are produced by multiplying the annual numbers of person-years of known seropositive and AIDS patients by ppy inpatient-day needs and cost estimates¹⁵. The assumption is made that stage-specific ppy needs and costs are stable over time, ensuring that any differences between 1993 and 2000 are due to changes in epidemiology.

Using the AIDS-impact model three scenarios are derived. The three epidemiological variants R, T and S result in, respectively, the reference scenario R, the therapy scenario T and subscenario S. As mentioned above, scenario S - the one referring to the smallest epidemic - describes the part of scenarios R and T estimating the potential impact on the hospitals based on only the HIV epidemic estimated for 1980-1990, also assuming no lengthening of AIDS survival.

Hospital inpatient-day needs are transformed into hospital bed needs using an occupancy rate of 90% [222]. Whenever appropriate, a discount rate of 5% for future monetary costs is used; this discount rate has been recommended for public sector

¹² The definitions classifying patients as CDC IV or AIDS are not completely identical. In presence of laboratory evidence of HIV infection, CDC IV encloses all types of AIDS (AIDS dementia, HIV wasting syndrome, specific cancers, and secondary infectious diseases of the AIDS surveillance definition) in CDC IVa, IVb, IVc-1 and IVd. Further the CDC-IV definition includes some secondary infectious diseases not resulting in the AIDS diagnosis (CDC IVc-2) and a rest-group (CDC IVe).

¹³ For one person it is assumed that person-years and observation-years coincide in the submodel stages of AIDS and known seropositive (known asymptomatic and symptomatic pre-AIDS).

¹⁴ The model assumes that every patient is at least a half year in the CDC-IV stage.

¹⁵ Following the literature on epidemiological modelling one may say that needs and costs in the last half year of the AIDS stage are modelled incidence-based; the incidence of death results in accounting costs to the preceding half year. Whereas, other costs are modelled prevalence-based; the presence of a patient at a particular point in time results in accounting costs. For prevalence-based modelling calculated prevalence halfway each year is used to give annual numbers of person-years for each particular stage.

analyses in the Dutch context [34,227].

Application of the AIDS-impact model is limited to the three main patient groups of homosexual men, intravenous drug users and heterosexuals. HIV infections due to mother-child transmission are excluded since both the incubation period and health-care resource utilization differ substantially for babies [228,229]. Up to June 30st 1993, 13 AIDS cases due to mother-child infections have been reported. Recipients of blood and blood products are excluded since their contribution to the future epidemic will be negligible due to the safeguarding of blood supplies. Finally 43 AIDS cases of unknown group adherence are not considered.

5.4 Results

5.4.1 Epidemiologic Results

Backcalculation of the infection curve shows a peak in the incidence of HIV infections in 1984 and 85 (Fig 5.2; presenting the infection curve as a three-yearly moving average). The epidemic among homosexual men dictates the overall pattern. The steep decrease since the mid-eighties is in line with the decline in incidence in an Amsterdam cohort of homosexual men [230]. However, recent studies by the Municipal Medical and Health Department of Amsterdam report possible resurgence in the infection curve for this group [231,232]. Since 1984 the estimated infection curves for intravenous drug users and heterosexuals both fluctuate around a level of 100 infections per year. The levels of HIV incidence in the period 1990-2000, as indicated by the assumption for R and T are 361 (homosexual men), 97 (intravenous drug users), 119 (heterosexuals) and 577 for the three groups together. By definition, scenario S does not incur new HIV infections in the 1990s.

For scenario R, a moderate increase is estimated in the prevalence in both AIDS and pre-AIDS stages (Fig* 5.3 and 5.4). For 1993, 1995 and 2000 June-30st levels are, respectively 1130, 1340 and 1620 for AIDS and 6480, 6610 and 6720 for pre-AIDS. In 1995 54% and in 2000 57% of pre-AIDS prevalence is known seropositive and is assumed to need hospital services. For 1993 the model estimates 51% to be aware of the positive serostatus, which is in line with HIV-testing results among homosexuals [233]. The proportion of homosexuals in pre-AIDS prevalence decreases from over 70% in 1993 to 65% in 2000.

Fig 5.2

Smoothed estimated annual incidence of HIV infections for the three main risk groups and their total (three-yearly moving averages): homosexual men (dots), intravenous drug users (boxes), heterosexuals (diamonds) and total (crosses)

Fig 5.3

Projected AIDS prevalence as of June 30st in scenarios R (dots), T (crosses) and S (triangles)

Fig 5.4

Projected pre-AIDS prevalence as of June 30st in scenarios R (dots), T (dots) and S (triangles)

In scenario S prevalences decrease. This is especially the case in the pre-AIDS stage (1993: 4480 with 65 % known seropositive; 1995: 3580 with 73 % known seropositive; 2000: 1800 with 87 % known seropositive). AIDS prevalence exhibits only a moderate decrease: 1110 halfway 1993, 1230 halfway 1995 and 1060 halfway 2000. In T pre-AIDS prevalence is of course analogous to that in R. In this scenario, AIDS prevalence, however reaches almost 2000 cases by the end of the century.

5.4.2 Economic Results

The 1995 projections of hospital bed needs amount to at least 150 beds in scenario S (Fig 5.5). Scenario T produces the highest estimate of bed needs at 170 beds in 1995. Despite a significant higher AIDS prevalence projection in scenario T relative to scenario R in 1995, bed needs for the two scenarios only deviate slightly. This is due to the assumption on the lengthening of survival so that only the *early*-CDC-IV phase, with relatively low inpatient-days needs, is prolonged. Bed needs projections for 2000 are 125 in scenario S and almost double this amount in scenario T (220 beds). Scenario R indicates a level of 195 beds.

Fig 5.5 *Projected hospital bed needs in 1995 and 2000 in scenarios R (black), T (light-grey) and S (dark-grey)*

Inclusion of monetary cost estimates for inpatient-care and inpatient-cure needs and need for outpatient facilities produces an overall hospital cost estimate of 33 800 thousand ECUs in 1993 (Fig 5.6). For 1995 projected hospital costs are of at least the same level as in 1993. The cost projections for scenarios R, T and S in 2000 are, respectively 45 600, 50 700 and 26 700 thousand ECUs.

Fig 5.6

Projected hospital costs in 1993 ECUs (inpatient care: grey; inpatient cure: boxes; outpatient facilities: black) in 1995 and 2000 in scenarios R (reference scenario), S (subscenario) and T (therapy scenario)

It is estimated that in 1993 inpatient care constituted 41% of total hospital costs, inpatient cure was 20% and outpatient facilities were 39%. Up to 2000, inpatient-care and -cure proportions are projected to increase in all scenarios (to 47% and 23%, respectively in scenario S), whilst a corresponding decline is projected for outpatient-facilities needs (to only 30% in scenario S). As most inpatient care and cure is required in the final phase of AIDS, where needs for outpatient facilities are low, this trend demonstrates the increasing importance of this stage in hospital cost projections.

5.5 Discussion and Conclusions

5.5.1 Epidemiologic assumptions

The epidemiological development underlying two of three scenarios is based on the assumption that no fundamental changes take place with respect to the recent level of HIV incidence. The average of the estimated incidences of 1987, 1988 and 1989 is applied to all future years up to 2000 (577 new infections per year). This epidemiological course indicates lower projections in the medium-term than the short-term projections presented earlier for The Netherlands. In 1987, Houweling *et al.* [234] estimated a prevalence of HIV-infected persons of 20 000. In 1990, Jager *et al.* [23] indicated a range for the prevalence of HIV-infected persons of 9000 to 13 000. The estimate of the prevalence of

HIV-infected persons as of January 1st 1990 amounts to 6630 (of which 630 are AIDS patients), which is in line with those reported by van de Water *et al.* [235]. Based on AIDS data as of December 1990, they estimated a prevalence of HIV-infected persons of approximately 7000 as of December 1988.

Underlying the AIDS-impact model is a backcalculation procedure. Recently backcalculation procedures have had to be adapted to take the effect of early treatment into account [92,210,236]. Prior to this adaption, backcalculating negative incidences of HIV infections have been attributed to the effect of early treatment [237,238]. Here, the effect of early treatment has been incorporated into the backcalculation procedure. However, as procedure is deterministic in nature negatives are not ruled out, although at the moment one does not encounter them. Further work will be directed to assessing the impact on health care, including a probabilistic mechanism for backcalculation (*see* for example, [239]).

The impact of AIDS is still very uncertain - this uncertainty is reflected in the construction of the scenarios. There remains a need to improve the reliability of data concerning the prevalence of persons with HIV infections, progression to AIDS and trends in HIV incidence. For example, clearly the scenarios are very sensitive to the incubation period distribution, since backcalculation and epidemiological projection are based on it¹⁶. The most recent insights from the literature are used and experts have been consulted in an attempt to overcome this lack of empirical data.

In contrast to the subscenario assumption, there will probably be a future spread of HIV infections. The impact of AIDS will therefore be more widespread than is the case in the subscenario. The HIV/AIDS incidence and prevalence in the reference scenario is greater than that produced by the subscenario and this difference increases over time, whilst the therapy scenario projects an even higher AIDS prevalence. The difference with the subscenario shows that continued efforts in the area of public education could prevent thousands of HIV infections and lower hospital resource utilization and corresponding costs significantly.

5.5.2 Economic Assumptions

The model projections are based on stable hospital inpatient-day needs per person-year (ppy) and stable ppy monetary costs of inpatient care and cure and outpatient facilities; in

¹⁶ This sensitivity is shown by Bloom&Gied [240] in an application to US-data.

other words stable treatment technology, intensity of care and prices are used. Further work could be directed to introducing trend developments into these parameters. A downward trend in ppy hospital inpatient-day utilization is reported [220]. Also, since a policy of substituting outpatient for inpatient care is favoured by the Dutch government [241], one might expect trends in hospital (and correspondingly non-hospital) resource utilization for HIV/AIDS. This development is present in the US [242,243]. For the Netherlands the development of a monitoring system for outpatient resource utilization and costs for HIV/AIDS has just started.

The model uses a single estimate of the costs per hospital inpatient day for *early-CDC-IV* and *late-CDC-IV*. In reality, it might be assumed that costs in the *late-CDC-IV* stage will be considerably higher due to more intensive care. In addition, the assumption is made that per observation-year (poy) hospital inpatient-cure and hospital outpatient costs have decreased in proportion to the decrease reported for poy hospital inpatient-care costs. As only partial information is available (information on trends in resource utilization but no information on costs [220]) to verify this assumption, it could be challenged, in particular for outpatient costs. Possibly, substitution of outpatient for inpatient activities has raised the importance of outpatient costs, relative to inpatient care costs.

Indeed, the reported decrease of poy hospital costs of care could be connected with increasing poy utilization of hospital outpatient facilities and corresponding costs. Assuming the poy decrease in inpatient-care costs for CDC-IV shifted completely to outpatient hospital services, this would raise hospital costs by less than 10% during the period 1991-2000 in each scenario. Obviously, this is a maximum estimate of the effect of substitution. Since one of the reasons for substituting outpatient for inpatient care is cost reduction, one expects lower rises in hospital outpatient costs. For CDC-II/III any significant effect seems to be absent altogether. So, the sensitivity of scenario results, concerning the assumption of proportional decrease of hospital outpatient costs, is only limited.

Finally, one should notice that the model projections are, at the moment, based on information on hospital resource utilization and corresponding costs of patients in the University Hospital Utrecht. At the moment it is unclear if this hospital is representative of HIV/AIDS hospital costs. Two other patient-based Dutch studies on HIV/AIDS hospital costs in Amsterdam are available: the Teaching Hospital of the University of Amsterdam [61] and Slotervaart Hospital [148]. Comparison of the Utrecht data with those of both Amsterdam studies is limited, due to differences in period of registration,

patient population, study design and measurement of monetary costs [62]. Only the Utrecht registration in Utrecht contains recent information on hospital resource utilization and costs. Since 1991 the registration has been extended to include further hospitals in Amsterdam, the Hague and Arnhem [244]. Comparative results of this multi-hospital study will be published shortly.

5.5.3 Comparative Analysis

It is estimated that hospital bed needs for HIV/AIDS are at maximum 220 and at minimum 125 in 2000. A recent study by RIVM produced some projections for hospital inpatient-day needs for selected diseases with a current major impact on hospital resource utilization [245,246]. As quantitative epidemiological data are often lacking, hospital inpatient-day needs projections for 2000 of lung cancer (ICD 162), diabetes (ICD 250), coronary heart disease (ICD 410-414), stroke (ICD 430-438) and pneumonia (ICD 480-486) are based on time series analysis of utilization data for 1980-1990 [247,248] (*see* Annex of this thesis). Time series analysis is performed on age- and sex-group-specific series of monthly standardized per capita hospital inpatient-day utilization (standard population is the average population in 1990). Including a factor for a sizable growth due to the aging of the population - as opposed to HIV/AIDS - for all five diseases, hospital bed needs projected for lung cancer, diabetes and pneumonia are approximately three- to fourfold that for HIV/AIDS, whereas those for coronary heart disease and stroke are over 10 times those for HIV/AIDS (Table 5.3).

Table 5.3 *Utilization of hospital beds in 1990 and projected bed needs in 2000 for lung cancer, diabetes, coronary heart disease, stroke and pneumonia*

	1990	2000
Lung cancer	634	610
Diabetes	840	660
Coronary heart disease	2400	2640
Stroke	1950	2210
Pneumonia	560	600

Source: SIG Health Care Information, Utrecht, the Netherlands; data processed by RIVM.

As demonstrated in the Annex of this thesis, projected decreases in the number of beds in 2000 for lung cancer and diabetes result from a sharp fall in the standardized

mean duration of stay in 1980-1990, whereas the standardized number of inpatient stays is fairly stable (lungcancer) or even decreasing (diabetes) in that same period. For diabetes the probable explanation is a substitution of outpatient care for hospital inpatient care. For pneumonia in 1980-1990 a sharp fall in the standardized mean duration of stay has been offset by an increasing standardized number of stays. A varied pattern for the different age and sex groups is found here: for elderly women and young boys the time series on bed utilization has a stable mean, for young girls the mean shows a significant decrease and for elderly men there is a significant increase in the mean. Finally, both diseases of the circulatory system show projected increases in the number of beds slightly below that which might be expected on the basis of demography alone. This pattern occurs as during 1980-1990 a fairly stable standardized mean duration of stay and number of stays (for stroke) and a decreasing standardized mean duration of stay combined with an increasing standardized number of stays (for coronary heart disease) results in a slight downward trend in standardized bed utilization.

Patient-related costs are the costs that can be attributed directly the treatment and care of patients with HIV and AIDS. Previously, the largest proportion of these costs was assessed to be associated with the hospitals [134]. For an updated comparison with other patient-related costs separate ppy monetary costs estimates for nursing home, district nursing, home help, general practitioner and intensive home care derived from an earlier report [101] and updated to 1993 prices, is used. As the Netherlands does not yet have an adequate system for registering outpatient and community care resource utilization, any cost estimate has to be based on fragmented research evidence.

The cost of AZT/zidovudine has typically represented a sizable proportion of the total costs in the AIDS stage [249], but now also represents a cost component in the pre-AIDS stages for early treatment. Unit costs are based on tariffs (nursing home, general practitioner and intensive home care), estimates of hourly cost prices (district nursing and home help) and market prices (AZT). Hospital costs are estimated to represent 85 % of total patient-related costs in 1993 (Fig 5.7). The general practitioner and home care (district nurse, mother's help and intensive home care) comprise a small share of total costs. Of non-hospital costs the use of AZT in early treatment represents the largest share.

Fig 5.7

Estimated distribution of patient-related costs (estimated 39 800 thousand 1993 ECUs) over various sectors in 1993: hospital; general practitioner (GP); nursing home; home care (mother's help, district nurse, intensive home care); and early treatment (with AZT)
Source: STG [101].

In addition to patient-related costs, there exists a range of general program costs. This costs division has proven to be useful in analyzing HIV/AIDS costs [2,156,250,251]. The general program costs due to HIV/AIDS can be estimated up to 26 million ECUs in the Netherlands in 1993. This amount is allocated between prevention (13 million ECUs, excluding AIDS prevention among dentists), research (5 million ECUs), HIV testing (5 million ECUs, with 80% for safeguarding the blood supply) and 3 million ECUs on planning and organisation [63,147,222,252].

An increase in hospital costs of HIV/AIDS is projected from 33.8 million ECUs in 1993 up to 50.7 million ECUs in the therapy scenario T for 2000 (price year: 1993). Using the average growth rates for the costs of Dutch hospitals in 1988-1993 (4.9%) hospital costs for all diseases in 2000 are projected to amount to 22 939 million ECUs [222]. In comparison, the costs in scenario T in 2000 of 66.3 million ECUs (price year: 2000; including an assumed yearly nominal growth rate of 3.9% in future years [222]), constitute 0.53% of the all diseases figure. The reference scenario R and subscenario S indicate lower shares (0.47% and 0.28%, respectively). Therefore, the scenarios demonstrate that approximately one quarter or a half percent of total hospital costs will be required for HIV/AIDS in the year 2000, a sizeable but probably manageable proportion.

Comparison of scenario R and scenario S provides insight into the potential gains from preventive efforts. Starting from the assumption that costs indicated by scenario S

are unavoidable, given unchanged treatment patterns, the excess costs of scenario R over scenario S increase from 6.0 million ECUs in 1995 to 22.1 million ECUs in 2000. Continuation or even an expansion of preventive efforts could counter this rise. If the most effective prevention programme resulted in an epidemiological outcome consistent with scenario S, the model implies, for the hospitals a potential preventive benefit of present valued 38 million ECUs for the years 1994-2000, relative to the reference scenario¹⁷. This represents 23 % of the present valued total costs of the latter. A considerable financial gain is possible through effective prevention, in addition to the human gains of reduced death and suffering. However, there remains unavoidable present valued costs 127 million ECUs for scenario S for the same period.

5.5.4 Summary of Results

- Projected hospital bed needs in the year 2000 of 125-220 for HIV/AIDS are limited compared to projections for coronary heart disease and stroke, but approach that for lung cancer, pneumonia and diabetes.
- Hospital costs are estimated to have caused 85 % of total health-care costs for HIV/AIDS in 1993. In 1993, the estimated proportions of hospital costs are 41 % for inpatient care, 20 % for inpatient cure and 39 % for outpatient facilities.
- The scenarios indicate a decreasing share of outpatient costs - possibly to 30 % of total hospital costs for HIV/AIDS in 2000 - illustrating the growing relative importance of the AIDS stage for the hospital costs. Hospital costs for HIV/AIDS in 2000 are projected to reach up to 0.52 % of projected hospital costs for all diseases.
- A present value of 38 million ECUs (23 %) of the hospital costs projected in the reference scenario might be avoidable, during the period 1994-2000. However, with unchanged treatment patterns a present value of 127 million ECUs of hospital costs during the same period is projected to represent unavoidable costs (discount rate: 5 %).
- In the Netherlands, data needs in the field of economic impact assessment of HIV/AIDS especially refer to registrations of non-hospital outpatient resource utilization and costs.

¹⁷ Following standard text books, when assuming benefits of preventive efforts, a discount rate to future monetary figures is applied [34]. So, in this paragraph cost figures are present values at 5 % discount rate.

At first sight, impact analysis by multiplying prevalence (or incidence) and hospital cost estimates seems to be a quite straightforward procedure. Due to differences by patient group affected, type of hospital care rendered, and stage of disease dealt with, however, as well as due to the spread of HIV infection, the quantification of current and future impact of HIV/AIDS on Dutch hospitals is quite a complex task. By integrating most recent and detailed data with respect to the above categories, this paper has achieved an important step in improving the current state of information. Nonetheless, uncertainty still remains, leaving issues such as national representativity, impact on other health-care sectors, and more accurate or even dynamic integration of treatment technology for future work. For the time being, an indication of the order of magnitude of AIDS impact on Dutch hospitals has been developed, and it is clear that HIV/AIDS will be on the agenda of hospital issues in the coming years.

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Chapter 6

A Life-insurance Fund for HIV-infected Persons; financial impact of expected future epidemiology

An extended version of this chapter was published as an RIVM-report (No 432501001 1994; Mogelijke Uitbreiding van het Garantiefonds voor HIV-geïnfecteerde Personen; financiële consequenties van verwachte epidemiologische ontwikkelingen) by MJ Postma, H Houweling, SH Heisterkamp and JC Jager

Management Summary

Objective: To assess the financial consequences of extending the Life-insurance Fund for HIV-infected haemophilia-patients to comprise all HIV-infected persons.

Data & Methods: Three types of data are used: (1) routine surveillance data on AIDS incidence by year of diagnosis, year of reporting, age and risk group; (2) interview data on income position of homosexual men from a study among readers of a national magazine; and (3) information on the need of several types of life insurance. Progression-of-disease (HIV infection, asymptomatic and symptomatic pre-AIDS disease, AIDS) is modelled by a multi-stage model. (Sub)stages of the model correspond to clinical classifications of HIV/AIDS and to the relevant stages for life-insurance need. A tentative analysis has been carried out by means of two scenarios on the financial consequences of the possible extension of the Life-insurance Fund.

Results: Extending the Life-insurance Fund, scenarios indicate an average extra yearly demand for life insurance, varying from f20.5 to 31.5 million. Demand is expressed in terms of insured amounts for three types of life insurance (pension, mortgage and temporary risk). Mortgage insurance is responsible for almost 80% of the amounts. A minimum demand of approximately f45 million is estimated for the homosexual risk group alone for the period 1995-1997.

Conclusion: Including future years up to 2005, premium-payments and discounting, the estimated size of the Extended Life-insurance Fund varies from f50 to 125 million.

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6.1 Introduction

The background of this study is the impact of HIV/AIDS on the life insurance-industry. In general, life insurers conceive persons with HIV/AIDS to be non-insurable with respect to insurances payable at death. For people with AIDS, insurers refer to the burning-house principle: insurance is impossible if the to be insured risk has already taken place. In general, persons with an increased risk of death are offered life insurance with increased premiums. For HIV, insurers have up to now indicated that the risk cannot yet be adequately estimated and accounted for in life-insurance calculations.

The non-insurability of persons with HIV has given rise to many discussions. Dutch insurers have urged for HIV-tests for insurance applicants. In addition, a code of behaviour has been defined that should lead to a restrictive testing policy of insurers. In short, the code specifies that an applicant for a life insurance below f200 000 (payable at death) can be demanded to be tested under certain circumstances¹⁸. Applicants for life insurance above f200 000 are always requested to have an HIV-test. Furthermore, insurers have the right to ask applicants whether they have AIDS or are HIV seropositive and to deny insurance for HIV-infected persons [253]. In the period March 1991-March 1992 nineteen persons applying for an insurance below f200 000 were tested, including one positive test [254].

The National Committee on AIDS Control (Nationale Commissie AIDS Bestrijding; NCAB) has urged that a provision should be developed to enable certain kinds of insurance for people who are aware of their HIV infection. This is to avoid the impossibility of full-participation in society for people who have several years of disability-free life still ahead. In particular, it is argued that life insurance is a "social good", as opposed to normal market commodities [255]. Social goods are thought to serve a social function and are instruments to secure a certain economic standard of living. In securing a decent standard of living for the dependants in the event of death, life insurance is essential. Then again, insurers claim that a less stringent code for HIV-infected persons is not in line with the probabilistic principles of insurance and point to the risk of self-selection, viz persons with a higher risk of death are tempted to apply for higher amounts of insurance [256,257].

For haemophilia-patients a provision has been designed by the Dutch Society of

¹⁸ The code specifies that the insurance company is allowed to ask some particular questions, such as "did you have a blood transfusion abroad?" and "do you use drugs intravenously?". Based on the answers the insurer can ask for an HIV-test.

Life Insurers (Nederlandse Vereniging van Levensverzekeraars; NVL) and the Dutch Red Cross, enabling the small-scale buying of life insurance. A lot of Dutch haemophilia-patients have been infected with HIV in the early days of the epidemic. The Ministry of Welfare, Public Health and Culture accounted for the financial part of the arrangement. In short, the provision enables haemophilia-patients to buy life insurance up to f200 000 without any restriction. If the insured person dies as a result of HIV/AIDS the insurance company involved is compensated out of the Life-insurance Fund (Garantiefonds). This provision has existed since January 1st 1993.

On June 1st 1993 the Secretary of State for Public Health, announced a study on the feasibility of extending the Life-insurance fund to encompass more persons at risk of HIV/AIDS. A study by NVL recommended a provision providing a benefit for relatives, but this has never been implemented [258]. Finally, NCAB has been asked to organize a feasibility study, covering important aspects such as epidemiological expectations and indications of possible sizes of the Extended Life-insurance Fund. Based on the experiences in the Dutch AIDS Scenario Study [101] on quantitative epidemiological aspects, modelling and financial-economic impact assessments RIVM was requested to perform this study, with NCAB merely acting as supervisor.

The need for life insurance depends on several personal aspects, such as age, income, housing, partnership and parenthood. Furthermore, the type of insurance is of importance, such as pension, mortgage, temporary risk and work-disability insurance. In general, life insurance serves two purposes. Life insurance can be of importance to secure financial independence for relatives (for example, to guarantee the financial means for housing in mortgage insurance). Furthermore, life insurance can be of importance for the insured person's participation in business if it is associated to a loan or credit. For example, having one's own business can be dependent on the possibility of obtaining a life-insured credit.

The nature of the Extended Life-insurance Fund restricts the scope of this chapter to those insurance types that are payable at death by the insurer. These types of insurance are payable if the insured person dies before the expiry-date, viz at premature death of the insured person. This study focuses on savings-mortgage, temporary risk and pension insurance. For the latter, in particular the widow and partner-components are important. Outside the scope of this study are life insurances that are payable at life at a specified end-date, such as a life-annuity, and work-disability insurance. In view of the complex discussions surrounding the general organisation of the latter type of insurance a separate study is recommended.

This study examines expected epidemiological developments in the short-term. In particular, the consequences in the first three years after an assumed extension of the Life-insurance Fund as of January 1st 1995 are estimated. For the years beyond 1997 a crude indication is provided.

6.2 Data and Assumptions

Epidemiology

The epidemiological data have been described in Chapter 5 of this thesis. Very brief, AIDS-registration as of June 30th 1993¹⁹ [219], and an average survival in the AIDS-stage of two years are used [14].

Income and housing

A specific study of the readers of a newspaper, directed at homosexual men (N=1199) provides insight into the income and housing circumstances of this AIDS risk group [259]. Table 6.1 summarizes some of the findings. Important findings were that 83.7% of those 25 years and younger have an income below f2000. Furthermore, of these 19.4% live with a steady partner. Steady partnerships occur in 20% of men aged 25 years and younger, 30% in men aged 26-35 and for 40% of men older than 35 years. As can be expected, the income distribution exhibits a "shift to the right" as age progresses. Almost 50% of men older than 40 years are in the upper income classes ($\geq$ f3000), and of these 45% has a steady partnership. In particular for the largest income class (f2000-3000) the percentage having a stable partnership remains similar as age progresses. In consequence, the general picture of an increase in steady partnerships seems to be related to the changing income distribution.

Of course, the representativeness of these data for all Dutch homosexual men can be questioned. Furthermore, due to lack of other sources, these data are also assumed for other AIDS risk groups, viz intravenous drug users and heterosexuals. Even more, representativeness of the data for these patient groups presents a problem. Below, all financial results are presented separately for homosexual men and for all risk groups together.

¹⁹ Haemophilia AIDS-patients and paediatric AIDS-cases due to vertical transmission are excluded as these groups are not intended to be reached by the Extended Life-insurance Fund.

Table 6.1 *Percentage distribution over net monthly incomes (in f) and per age-category (between brackets the percentage is shown of persons living with a steady partner)*

Income	≤ 2000	2000-3000	3000-4000	≥ 4000	total
Age					
≤ 25	83.7 (19.4)	14.0 (25.0)	1.2 (0.0)	1.2 (0.0)	100 (19.8)
26-30	44.6 (34.0)	44.2 (33.3)	9.4 (28.6)	1.8 (75.0)	100 (33.9)
31-35	26.2 (24.1)	49.0 (31.7)	18.0 (27.0)	6.8 (42.9)	100 (29.6)
36-40	23.0 (38.3)	45.1 (33.7)	21.1 (41.5)	11.8 (62.5)	100 (39.7)
≥ 40	17.5 (28.6)	32.8 (33.1)	29.9 (45.5)	19.8 (46.3)	100 (38.6)

Source: [259]; data processed by RIVM.

*Life insurance*²⁰

This section specifies the assumptions used to assess the relationship between personal circumstances and the desired level of each selected type of life insurance.

Of persons without a steady partnership 20% are assumed to buy their own house, and a connected savings-mortgage insurance. For those living together with a steady partner this percentage is assumed 40%. These supposedly conservative estimates are thought to reflect the scarcity of own homes in Amsterdam, where the majority of HIV seropositives live. The "rule-of-thumb"²¹ in determining life insurance is that the insured amount equals two and a half times gross income in paid employment, and twice gross income in self-employment.

For persons who are aware of their HIV seropositivity, 10% are known to be self-employed [260]. It is assumed that 50% of self-employed HIV-seropositive persons are in need of a temporary risk insurance connected to business credit. Furthermore, it is assumed that those living with a steady partner, wish to buy this type of life insurance for their partner (the "classical type" of life insurance in the Hollywood-movies). It is assumed that 80% of the self-employed and 30% of the paid-employees buy temporary risk insurance for their partners. Obviously, paid-employees without a steady partner are in no need for this type of insurance. The general rule in life insurance equals a temporary

²⁰ This section is designed in cooperation with W de Boer MSc, who is a member of the AIDS-research committee of the Dutch Society of Insurers (Nederlands Verbond van Verzekeraars).

²¹ Of course in practice, one might deviate from the "rule-of-thumb" calculus, when for example a smaller amount is sufficient.

risk insured amount to gross income (in paid employment) or half of gross income (in self-employment).

Partner-pension insurance is considered indispensable for self-employed persons in a steady partnership. The formula for the insured amount operates on the amount of gross income above f25 000. The amount is halved to arrive at the usual level of the pension and multiplied by a factor 20 to approximate an indexed unit of partner pension; viz insured amount equals: $(\text{gross income} - 25.000) * 0,5 * 20$.

Finally, the point of departure has to be assessed for estimating actual demands for life insurance. In particular, a part of life insurance needs might have already been covered in the past. For example, a person might have purchased his own house prior to seropositivity. As no adequate information is available, crude assumptions are applied. Obviously, the older the person is, the greater the proportion of total needs already covered will be. It is assumed that those aged 40+ already have 75% covered, those aged 35-39 already have 50% covered, those aged 30-34 already have 25% covered and the rest has no coverage yet. Obviously, for the last group demand equals need.

6.3 Method

Epidemiology

The progression-of-disease model has been described in detail in Chapter 5 (Fig 5.1). Here, it is recalled that five stages are distinguished: acute infection, asymptomatic HIV infection, symptomatic pre-AIDS disease and AIDS. Furthermore, asymptomatics are separated into two groups, depending on whether HIV-infection status is known or unknown. The combined stages of known asymptomatic and symptomatic pre-AIDS will be referred to as the stage of known seropositive. The combined stages of acute infection and unknown asymptomatic will be referred to as the unknown seropositive stage. This difference in unknown and known is crucial for insurance purposes: knowledge of one's seropositivity should be specified on the life-insurance application form, resulting in denial of access to insurances that are payable at death. This means that known seropositives are likely to have major problems in buying life insurance. As explained in Chapter 5, the progression-of-disease model is combined with a backcalculation procedure on AIDS surveillance data to estimate past incidence of HIV infections.

For the future, assumptions are specified for HIV infections, resulting in the reference and the subscenario. The influx of estimated past and assumed future incidence

of HIV infections, the flow through the different disease stages and AIDS-related deaths determine the incidence and prevalence of known seropositives (compare Fig^s 5.2 and 5.4). Known seropositives can be assumed to have been denied life insurance in the past or have refrained from attempts to buy insurance, knowing that denial is likely. On the other hand, unknown seropositives can be assumed to often have been able to buy insurance through regular channels. Therefore, only the needs and demands for life insurance of known seropositives are specified.

The subscenario reflects a part of the reference by calculating only the consequences of incidence of HIV infections before 1990 ("unavoidable epidemic"). In particular, persons infected before 1990 can have experienced problems in their access to the life-insurance market. Recently infected persons have only experienced this blockade for a relatively few years and might already have covered a lot of insurance needs before infection. Summarizing, the demand for life insurance can be conceived as a function of age-related income increases (higher age/income induces higher demand), age-related proportion of need already covered (higher proportion covered lowers demand) and duration of seropositivity (longer durations are related to higher demands). As such, the method integrates these different relationships by using age-dependent needs and age-dependent proportions of covered needs in combination with different scenarios. Obviously, age should be the variable to relate epidemiology to life-insurance needs/demand.

Linking epidemiology and life insurance

The epidemiological projections can be readily extended with an estimate of the age distribution of incidence and prevalence in the various stages. As a basis the age distribution of cumulative AIDS incidence at June 30st 1993 is taken. This distribution is assumed to be stable over the years. Age-specific prevalence of known seropositives is directly transferable into a distribution of known seropositives according to income and housing circumstances, using Table 6.1. As mentioned, income and housing are assumed to determine the need for life insurance²².

²² To transform net monthly income from Table 6.1 to gross annual income the next table is used:

Table *Gross annual income per net monthly income (in 1990 f) and housing situation (gross annual income is based on the midpoints of the net income intervals)*

	Without partner	With partner
Net monthly income < = 2000	35 000	30 000

To determine the need for life insurance the prevalences as of the beginnings of 1995, 1996 and 1997 are used. To translate needs into actual demand it is taken into account that life insurances can be obtained up to f200 000 per person (aggregated over the three forms of insurance considered). This is conform the design of the Life-insurance Fund for haemophilia-patients. The model therefore cuts off individual demands at a maximum of f200 000. Extension of the Life-insurance Fund as of January 1st 1995 would mean that life insurance needs of the present known seropositives become actual. This results in a demand for life insurance. It is assumed that in the first year (1995) one third of uncovered needs is actually demanded. In 1996 and 1997 again one third is demanded. This even spread of demand over three successive years is rather arbitrarily. Progression to AIDS might prevent demand, as the Extended Life-insurance Fund does not apply to AIDS patients. Their needs remain uninsurable. For the new known seropositives of January 1st 1996 and 1997 the same rule of "even spread" applies. Thus, the additional needs due to incidence of known seropositives in 1995 and 1996 are taken into account, viz unknown seropositives as of 01 01 1995 who become aware of their serostatus in 1995 and 1996.

Table 6.2 *Projected prevalence as of January 1st in Reference and Subscenario (the latter between brackets): Total (all patient groups*) and Homosexual men only**; all (known and unknown seropositives) and known seropositives only*

			1994	1995	1996	1997
Total	all		6620 (3872)	6673 (3429)	6712 (3014)	6739 (2631)
	known		3445 (2780)	3567 (2579)	3653 (2364)	3727 (2149)
Homosexual	all		4606 (2843)	4579 (2512)	4547 (2204)	4512 (1920)
	known		2503 (2063)	2551 (1905)	2571 (1742)	2587 (1579)

* Excluding haemophilia-patients and vertical transmission; ** Including intravenous drug using homosexual men.

2000-3000	45 000	40 000
3000-4000	70 000	65 000
> = 4000	110 000	100 000

Table 6.3 *Age distribution of AIDS (as of June 30st 1993) and HIV incidence (estimated; assumed stable during time) for all patient groups* (between brackets: homosexual men only**)*

	AIDS	HIV
< = 19	0.3 (0.0)	10.7 (9.6)
20-24	2.7 (2.1)	18.1 (17.1)
25-29	14.0 (13.4)	21.3 (21.1)
30-34	22.0 (20.4)	19.0 (20.5)
35-39	20.8 (21.9)	14.0 (15.4)
40-44	17.4 (19.6)	8.0 (8.5)
45-49	11.0 (12.0)	4.4 (4.2)
50-54	5.3 (5.5)	3.1 (2.5)
55-59	3.6 (3.1)	1.4 (1.0)
> = 60	2.8 (2.1)	0.0 (0.0)***

* Excluding haemophilia-patients and vertical transmission; ** Including intravenous drug using homosexual men; *** By assumption.

Source: GHI [219]; data processed by RIVM.

Table 6.4 *Estimated age distribution as of January 1st 1994 in the Reference scenario of total pre-AIDS prevalence and known seropositives only, for all patient groups* (between brackets: homosexual men only**)*

	Total	Known
< = 19	4.3 (3.2)	2.7 (1.8)
20-24	8.7 (7.6)	5.9 (5.0)
25-29	15.7 (14.4)	13.5 (12.3)
30-34	19.5 (19.3)	19.3 (18.6)
35-39	18.4 (19.5)	19.7 (20.4)
40-44	14.2 (15.8)	16.0 (17.7)
45-49	9.2 (10.3)	10.8 (12.1)
50-54	5.4 (5.6)	6.2 (6.6)
55-59	3.1 (2.9)	3.7 (3.5)
> = 60	1.6 (1.4)	2.2 (1.8)

* Excluding haemophilia-patients and vertical transmission; ** Including intravenous drug using homosexual men.

Table 6.5 *Estimated age distribution as of January 1st 1994 in the Subscenario of total pre-AIDS prevalence and known seropositives only, for all patient groups* (between brackets: homosexual men only*)*

	Total	Known
< = 19	2.0 (1.2)	2.0 (1.2)
20-24	5.0 (4.3)	4.5 (3.8)
25-29	13.1 (11.9)	12.4 (11.3)
30-34	19.5 (18.7)	19.2 (18.3)
35-39	20.1 (20.8)	20.3 (20.8)
40-44	16.6 (18.3)	17.0 (18.7)
45-49	11.2 (12.5)	11.7 (13.0)
50-54	6.4 (6.8)	6.7 (7.1)
55-59	3.8 (3.6)	3.9 (3.7)
> = 60	2.3 (1.9)	2.4 (2.0)

* Excluding haemophilia-patients and vertical transmission; * Including intravenous drug using homosexual men.

6.4 Results and Discussion

Epidemiology

Table 6.2 shows projected prevalences in the pre-AIDS stages. In the Reference scenario, the percentage of known seropositives in all seropositives ranges from 52% in 1994 (all risk groups) to 57% in 1997 (homosexual men only). In the Subscenario, the percentage of known seropositives increases from 68% in 1994 to 82% in 1997. Tables 6.3 through 6.5 show the age distributions of incidence and pre-AIDS prevalences in both scenarios. Table 6.3 illustrates the difference in the age distributions of HIV and AIDS, that currently amounts to more than 8 years in average. In the long-term and under specific conditions this difference will approach the average incubation period of 12 years. Almost 80% of HIV incidence is in persons below 40 years and almost 60% is for persons between 20 and 35 years of age.

Tables 6.4 and 6.5 indicate that the group of known seropositives has an average age that is of course higher than that of the average seropositive, viz known seropositives are up to 3.2 years (homosexual men in the Reference scenario) older than unknown seropositives. Obviously, this difference is in line with the durations of both stages of unknown and known seropositive, and will in the long-term and under specific conditions approach 6 years. Estimated age distributions for January 1st in later years are rather

similar in the Reference scenario. In the Subscenario, the average age roughly increases by one year per year passing.

Recently, the number of HIV-infected homosexual men during the early nineties has been estimated at 6500 to 15 000 by Wiessing *et al.* [233]. The estimates (Table 6.2) are obviously below the lower bound of this estimate. Other than the backcalculation approach for estimating HIV prevalence, in [233] seroprevalence is estimated through a direct method, based on the data from [259]. In line with the analysis, the proportion of known seropositives in [233] is estimated at 50%.

As explained in Chapter 5, the backcalculation approach used is a deterministic one. This implies that, for example, negative estimates of HIV incidence are not excluded at forehand, although at the moment they are not encountered. But in general, the model doesn't separate incidental fluctuations from structural developments. To confront this general flaw in the model a new method has recently been developed [239]²³.

Application of the model to the Dutch situation implies cumulative HIV incidence of 6510 per as of January 1st 1990 among the three major risk groups: homosexual men, intravenous drug users and heterosexuals. For comparison, in the above analysis the corresponding figure is 7140. Also the most recent estimated level of new HIV infections is lower in Heisterkamp *et al.* [262]. The current estimate and input for the Reference scenario amounts to 579 new HIV infections per year. In [262] only 180 new infections annually are estimated. Although large confidence intervals are indicated, the possibility should be considered of significantly lower levels of HIV incidence than currently underlying the Reference scenario. Finally, the estimate for January 1st 1994 of pre-AIDS prevalence amounts to 4260 in [262], which is between the Reference and Subscenario estimates. An analogous partition of the incubation period produces an estimate of 68% known seropositive, corresponding with the Subscenario.

Scenarios for life insurance demand

Life insurance demands of known seropositives in the years 1995, 1996 and 1997 are respectively f30.4, 31.6 and 32.7 million in the Reference scenario and f23.2, 20.4 and 17.7 million in the Subscenario. Comparison of both scenarios indicates that more than three quarters of demand come from persons infected with HIV before 1990. As mentioned, to this part of demand a higher likelihood is assigned than to the rest. Of

²³ No specifically defined functional relationship for incidence of HIV infections is assumed. As in [261] a stylized pattern for HIV incidence is applied: incidence in one year is not allowed to substantially deviate from those in surrounding years.

course, in 1997 the share of the Subscenario in the Reference scenario is smaller (just over 50%) than in both previous years. Homosexual men account for 67-74% of demand. Furthermore, the shares of savings-mortgage, business temporary-risk, partner temporary-risk and pension insurance are quite stable at respectively 80%, 3%, 10% and 7%.

Life insurance demands in the Subscenario reflect those of known seropositives who might possibly have been blocked for several years in their access to the life-insurance market. They have been seropositive for at least five years and might be "waiting" for an Extended Life-insurance Fund. The probability of the realisation of this part of demand is therefore high. This part is 50-75% of the Reference scenario. Furthermore, reasoning that intravenous drug users might buy less life insurance even under the new Extended Fund, an expected *minimum demand* of approximately f45 million is estimated for homosexual men in the Subscenario during 1995-97.

For the years after 1997 a significantly lower demand is estimated, as the "catch-up" demand of the large group of known seropositives prevalent as of January 1st 1995 is assumed to take place during 1995, 96 and 97. For the years after 1997 only the needs of the new incident known seropositives and the changes in needs due to progression in age and in disease are of relevance. The Reference scenario assumes 579 new HIV infections annually, corresponding to an annual demand for life insurance of approximately f15 million. In the Subscenario demand decreases from f2 million to a negligible amount in 2005.

6.5 Conclusion and International Comparison

For an integrative estimate for the total size of the Extended Life-insurance Fund one has to cover two further aspects: premium-payments and discounting. The former aspect would at a maximum allow a lowering of the Extended Fund by 10%, as the vast majority of the HIV-infected persons are aged between 25 and 45 years, and premiums are relatively low for this age group. Furthermore, premiums will only be paid for a period in the order of magnitude of the incubation period. A discount rate has to be used to recalculate all monetary amounts into their present value. As in the previous Chapter a 5% rate is used. Including a 10%-lowering due to premium-payments and discounting the Reference scenario and Subscenario indicate funds of respectively f125 and f50 million to cover demands in the period 1995-2005. For comparison, the current (non-extended) Life-

insurance Fund is $\text{f}5$ million.

It may be that demand is lower than that considered here. For example, several HIV-infected persons might have attracted funds through other channels, such as personal loans. Furthermore, the general calculus rules in life insurance might very well indicate amounts above those that are necessary. As mentioned, intravenous drug users might have significantly lower needs and demands than the income and housing data for homosexual men indicate. On the other hand the construction of the Extended Life-insurance Fund could stimulate the willingness to be HIV-tested, increasing the number of known seropositives in the short-term. However, perhaps the most serious caveat for the new fund is the Dutch membership of the European Single Market. Non-Dutch HIV-seropositive European citizens could start buying life insurance in the Netherlands. HIV prevalence rates in several other EU-countries such as Spain, France and Italy are several times that in the Netherlands. Exclusion from the Extended Life-insurance Fund of non-Dutch applicants has been argued to be difficult [263]. These legal aspects are not further elaborated here.

Of course, the same discussions exist in other European countries and elsewhere life insurances are denied to HIV-infected applicants, HIV-tests are required and specific questions are asked. For example, in the UK a lot of concern has been generated by a policy of denying life insurance to anyone ever having had an HIV-test or even for just belonging to a high-risk group. Furthermore, large companies generally require a test for all amounts over £40 000 for single males, compared to much higher limits for others [264]. In Belgium, France and Italy applicants for amounts over respectively BF5 million, FF1 million and ITL300 million are required to have an HIV-test. In Germany applicants for amounts over DM250 000 are medically examined, this may include an HIV-test. In France, the code of conduct in life insurance prohibits questions into the applicant's private life, whereas in Sweden the entire private life should be discussed with a physician [265,266]. Obviously, because of some strict regulations elsewhere, HIV seropositives from abroad might try to seek insurance through an extended Dutch Life-insurance Fund. In consequence, from this international perspective, we should note that the potential number of HIV seropositives who might come to the Netherlands is substantial and could further burden the Extended Fund.

Chapter 7

Disease-staging and Cost-standardization for Modelling Health-care Impact of HIV/AIDS

The first part of this chapter was published by MJ Postma, JC Jager, D Ruwaard, NCM van Loy, RM Leidl as a part of **Disease-staging for Modelling Current and Future Health-care Impact of Disease; illustrations for Diabetes mellitus and AIDS** (*Health Policy* 1998, 43:45-54); reprinted with permission

The second part of this chapter is based on **A Standardized Costing Framework for HIV/AIDS Hospital Care in the European Union** by K Tolley, MJ Postma, JC Jager, M Good in: J Kyriopoulos *et al.* (Eds) *AIDS Cost Analysis and Patient Classification* (in press)

Abstract

This paper addresses the economic relevance of appropriately staging progression-of-disease for cost assessment and future projection. An illustration is drawn from a Dutch cost-of-illness study for AIDS. The disease staging specifies a separate late stage to capture terminal high-intensity care for end-stage complications. Data are used from a detailed database on AIDS hospital care and costs. Neglecting the separation of a specific late stage is estimated to overestimate hospital bed needs for AIDS in the Netherlands by almost 15%. In particular, confidence intervals of future projections for AIDS hospital beds - using respectively staged and non-staged models - do not overlap. AIDS hospital costs are overprojected by almost 11% in the non-staged model. In conclusion, an appropriate disease-staging averts structural biases in estimations of bed needs and costs, and therefore benefits the planning of hospital care facilities.

Obviously, specific disease-staging requires reliable and detailed data on hospital care and costs, preferably drawn from databases. A standardized approach in gathering this information would allow the extension of the Dutch methodology to other countries. For the purpose of extending the method to the EU as a whole, criteria and recommendations are specified in the Standardized Hospital Costing Framework.

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7.1 Introduction

Cost-of-illness studies form one of the starting points of health economics thinking. These type of studies typically address the costs on society of particular diseases that are of specific interest. Generally, two motivations for performing such studies emerge [3,267]: (1) to assess the current health-care burden of disease on society (some Dutch examples are [246,268]); (2) to define parameter values for projecting future health-care burden of disease (two Dutch examples are [62,269]). Estimates of current and future burden of disease attribute to health-policy making, in particular to the planning of care services. This chapter addresses the economic relevance of appropriately staging progression of disease and the need for standardizing the methodology for cost-of-illness studies. In particular, this chapter focuses on cost-of-illness studies of HIV/AIDS in the European Union and derives some specific results for one Dutch cost-of-illness study. This chapter builds on previous publications on this topic [66,101].

This chapter extends work conducted in the framework of the Dutch Steering Committee on Future Health Scenarios, which has guided many research projects in the fields of health and health care [146]. Examples on AIDS will be used to illustrate the importance of appropriately staging progression-of-disease for averting biases in projections of future health-care needs and costs. Stages of disease should be chosen such that individual stages reflect important differences in the intensity of resource utilization, needs and corresponding costs. Furthermore, this chapter elaborates on the EU-project "Managing the Costs of HIV Infection" (EU-project SOC 94 20018005F01) [95,96]. This project developed the so-called "Standardised Hospital Costing Framework for HIV/AIDS treatment and care" (SHCF). The explicit use of standards in this field helps improve the quality of methods in resource utilization measurement and cost studies and enhances the comparability of estimates produced. Thus, usefulness of the estimates is maximized for a range of research and policy purposes at the local, national and multi-national (European Union) levels.

7.2 Disease-staging of HIV/AIDS

In the previous chapters estimates of the current impact of HIV/AIDS on hospital bed needs and hospital costs and future scenarios thereof were presented. Hospital costs included those of inpatient care and cure and utilization of outpatient facilities. In addition to the Dutch results presented in chapter 5, the contributions to hospital bed needs and hospital costs of pre-AIDS and AIDS stages in the Reference scenario can be examined in more detail (Fig 7.1). A clear overall decreasing pattern is exhibited in the percentage of pre-AIDS in total bed needs and costs. In particular in the beginning of the epidemic, the number of persons in the pre-AIDS stage is relatively high as compared to the number of persons with AIDS (PWAs). Both indicators decrease from 100% in 1980, through 34% (beds) and 70% (costs) in 1985 to 9% (beds) and 28% (costs) in 2000. In the Subscenario and the Therapy scenario the decrease of the share of pre-AIDS in the total is even steeper.

Fig 7.1 *Percentage of hospital beds (solid line) and hospital costs (interrupted line) for pre-AIDS of respective totals for HIV/AIDS*

In chapter 5 progression of AIDS disease was staged into two subcategories: the final half year of AIDS preceding death (*late stage*) and the foregoing period (*early/chronic stage*) [270]. Summarizing chapter 5 its findings, the costs per person-year (ppy) in the late stage are almost three times those in the chronic stage (Fig 7.2). Furthermore, more than half of lifetime hospitalization costs are generated in the late stage. Also, the intensity of hospital inpatient days utilization in the late stage appeared to

be almost four times that in the chronic stage (94 versus 25 days). Similar findings are reported in the American literature [271-273]. For example, one study shows that hospitalization costs in 1990-91 for PWAs rise sharply in the final half year prior to death up to US\$23 000, compared to below US\$7000 in other sixmonthly periods [273].

Fig 7.2 *Hospital inpatient-day utilization (grey; left axis) and hospital costs (black; right axis) per person-year (ppy) in the chronic and late stage of AIDS (see text for definition of stages)*

Using the data from Fig 7.2 and an AIDS-survival of 3 years in average, lifetime hospital bed needs and hospital costs can be derived for a hypothetical cohort of 1000 incident PWAs in the Netherlands (Fig 7.3, light bars; for the derivation of confidence limits, see chapter 9)²⁴. Average AIDS survival has increased from one year in the beginning of the epidemic to two years currently and might be assumed to further increase to three. Improvements in survival prolong the chronic stage, thus raising the relative importance of resource needs and costs in this less-resource-intensive and relatively cheap stage, compared to the late stage. A non-staged AIDS-disease model would not be able to grasp this changing relative importance of both stages (Fig 7.3, dark bars). The non-staged model overprojects future hospital bed needs; the 95%-confidence intervals of both models do not overlap. A similar result was found for hospital costs, with the 60.4 million ECUs according to the staged model not included in the 95%-confidence interval of the non-staged model's projection. In consequence, it has been

²⁴ The incidence-based approach is used for linking epidemiology and health care [274] and an occupancy rate of 85% is applied for transforming hospital inpatient days to hospital beds [275].

shown that the choice of an appropriate disease-staging averts structural biases in projections of AIDS health-care impacts.

Fig 7.3 *Lifetime hospital bed needs and costs (survival in AIDS stage of 3 years) according to a staged model (light) and a non-staged model (dark), including 95%-confidence intervals*

7.3 Standardised Hospital Costing Framework (SHCF)

Extending the Dutch scenarios of the previous section to other countries and the multinational EU-level involves an investigation for suitable and comparable information sources on HIV/AIDS hospital resource utilization and costs. To enhance comparability the SHCF has been developed [276]. As a part of the SHCF five specific fields for standardization of such studies are identified. (1) Information should be detectable from a sufficiently large patient sample size in the relevant disease-stages and sufficient patient follow-up for recording resource utilization and costs should be ensured. (2) To produce representative estimates for national and regional planning purposes a sufficient number of the main treatment sites covering the country/region should be included. (3) The possibility to break down aggregates so as to identify the contribution of different components of care in the care and cost totals should be supplied. (4) The possibility should be build-in to produce homogeneous cost groups, for example using several classifications such as CDC-stages [16,17], Turner-stages [277,278] or specific disease-staging definitions as late versus early/chronic AIDS. (5) Finally, a standardised methodology in approach and presentation should be followed to enable the effect of "true factors" to be identified (differences in epidemics, health-care structure and practice,

pricing structures and local health-care labour markets). The SHCF is intended to provide recommendations in these five fields of standardization and could possibly serve as a clearing house for designing studies in HIV/AIDS resource utilization and costs.

The SHCF is in essence a hierarchy of technical "accounting" steps associated with estimation of mean resource utilization and costs per person-year for pre-AIDS stages, AIDS-stage, specific episodes and of the lifetime resources and costs. The accounting framework is grounded on a number of elements of standard economic costing practice. Five main standards were used to develop the SHCF. (1) As a starting point, clarification of the perspective of the evaluation should be provided, viz the hospital or the health services planner at the national or multinational (EU) level. (2) Next, cost components and resource utilization units should be identified according to the perspective adopted. The framework covers four standard cost components, viz inpatient, outpatient, day care (inpatient for several days with no overnight stay) and day case (admitted and discharged in one day). For specific purposes the last two or three components are taken together as respectively day care and outpatient care. (3) For measurement of physical resource utilization rigorous methods of study design and data collection are essential, viz predominantly patient-based (bottom-up) assessment of resources should be pursued. (4) Valuation of resources should be done using appropriate methods of unit cost (or price) estimation that closest reflects opportunity cost, viz caution must be exercised in using health-service charges or tariffs. (5) Production and presentation of mean resource and cost estimates should be according to the decision-making context for which they are to be applied (total, AIDS-stage, pre-AIDS stages, clinical condition or transmission group). Together, the accounting framework and the standard principles that it is based on - if adopted in new cost studies - should produce cost estimates that compared to previous studies more meet the normative criteria of good quality and comparability.

The SHCF has both retrospective and prospective applications. Retrospectively, it can be used to enable assessments of the quality and comparability of estimates from previous studies. Through this application it illustrates the level of detail for which meaningful comparisons from existing studies are possible. An example, from a review of EU cost studies published between 1985-95 is presented in Table 7.1. In general, it is possible to make comparisons of hospital inpatient care for AIDS, and to a very limited extent for outpatient care and pre-AIDS care. Prospectively, the SHCF provides standards from which recommendations for new HIV/AIDS costing studies can be developed.

Table 7.1 *Overview of studies on hospital resource utilization and costs: country, reference, study size in patients and inpatient days per person-year (ppy)*

Country	Reference	Study period	Size	Inpatient days ppy
Belgium	[190]	1987-88	24	106
Denmark	[279]	1980-86	33	-*
France	[56]	1986	100 ⁺	-
	[280]	1986	35	-
	[281]	1988-93	2800	41
Germany	[191]	1985-86	± 29	66
	[59]	1985-87	10	130
Greece	[192]	1988	7	110
	[282]	1988-91	60	27
	[283]	1990-91	105	13
Italy	[284]	1984-88	51	185
	[285]	1985-88	77	99
	[65]	1990-91	68	47
Netherlands	[62]	1982-88	230	58
	[62]	1989	79	513 [†]
	[220]	1987-90	126	28-90 [‡]
	[270]	1988-92	296.6 [®]	29 [‡]
Portugal	[214]	1991	96	22
Spain	[193]	1987	6.3 [®]	130
	[193]	1987	8.5 [®]	105
	[212]	1990	156	26
UK	[55]	1985-86	16	90
	[194]	1989	12	-
	[286]	1982-90	459	33
	[287]	1984-92	187	-
	[288]	1991-93	60	24
	[289]	1983-90	354.8 [®]	31-92

* Not reported; ⁺ Admissions; [‡] Figure refers to CDC IV; [®] In person-years.

7.4 Discussion and Conclusions

This paper has illustrated that the choice of an appropriate disease-staging averts structural biases in projections. Obviously, a first staging of HIV-disease in an AIDS and a pre-AIDS stage is essential. The dynamics of the HIV/AIDS epidemic causes the distribution of HIV-infected persons over these two stages to change continuously. In combination with major differences in resource needs and associated costs between these stages, these dynamics have major implications for aggregate resource needs and costs. The illustration has shown that the miscalculation in projecting future health care impact of AIDS neglecting pre-AIDS stages is less serious for the hospital resource needs than for the hospital costs. This is an important finding, in view of the lack of accurate data on the health care utilization in these pre-AIDS stages in most countries [95]. Furthermore, it has been illustrated that a further substaging within the AIDS-stage in a chronic and a late stage is crucial for averting structural biases in future projections. In consequence, any extension of the scenario methodology to other countries and regions, such as the European Union, should control for disease-staging.

As studies on Medicare-patients in the USA show, the concept of a relatively expensive late stage for AIDS can be extrapolated to other diseases. Overall, ppy health-care costs in the last *whole* year of life are 6.8 times those in other stages of disease [290,291]. Sector and death-cause specific results show that the difference is particularly high for hospital costs of cancer (12.2) and respiratory diseases (11.2). Furthermore, a similar pattern is reported for ppy hospital discharges. Some further details of this study enable us to calculate the overall costs in last *half year* of life, that appears to cause 80% of the costs in the last *whole* year (Fig 7.4). For comparative purposes the AIDS-staging is included, showing that the difference must be much more pronounced for several other diseases. Consequently, neglectation of a resource-intensive and costly late stage in modelling other diseases - such as respiratory diseases and cancer - might introduce serious biases there as well.

Fig 7.4

Hospital costs for AIDS in ECUs (grey; left axis) compared to Medicare costs in US\$ (black; right axis) per person-year (ppy) in the late stage (last half year of life) and its complementary chronic stage (sources [270] for AIDS; [291] for Medicare)

Methodologically, further refinement of the staging-mechanism can be pursued.

Currently, the most important refinement would concern the explicit modelling of health-care needs for "short-survivors". On a per person-year basis in the late stage, persons with AIDS surviving less than a half year have been shown to be admitted to hospital four times as often than persons with AIDS surviving longer than a half year (Fig 7.5; [292,293]). Furthermore, the staging concept can be extended to other diseases. For example, in modelling the costs of diabetes mellitus one could consider the separation of an expensive late stage, reflecting resource needs and costs of complications that may occur many years after the onset of the diabetes [294]. Also, gathering comparable information and developing similar methodology on diseases, such as respiratory disease, cardiovascular disease and cancer, is needed and could benefit policy decisions in these fields. This staging of disease for economic reasons can follow different strategies, depending on study purpose, disease characteristic and data availability; they typically have to be developed, motivated and tested just as any other analytical concept in economic evaluation.

Fig 7.5

Hospital inpatient stays during the whole stage (light; left axis) and per person-year (dark; right axis): CS - chronic stage; LS1 - late stage with a duration of stay of 0.5 year; LS2 - late stage with a duration of stay below 0.5 year (see text)

Obviously, the type of analysis requires a rather detailed patient-based registration, that is ideally set-up with the purpose of providing information for cost-of-illness and future projections. Furthermore, the type of information required can only be retrieved from bottom-up patient-based data on health-care resource utilization and costs, in case of time-related staging of disease with a documentation over the full life span of a specific patient. This detailed information enables us to provide cost-of-illness assessments in the present and in future projections supporting health-policy decisions. They provide a quantitative order of magnitude for health-care resources. They specify the patient-mix for example in terms of chronic and late, which is an important indicator for planning hospital staff and capacity.

The SHCF can help in designing bottom-up patient-based costing studies that render the appropriate information. If SHCF-standards are followed the information that is necessary for cost assessment and projection is identifiable. Further application of the SHCF could involve the examination of local, national and multi-national variations in hospital resource utilization. If bias due to methodological differences is minimised, cost variations due to differences in clinical practice, health-care structure and organisation and epidemiology can be more readily identified. In addition, the SHCF-standards should improve investigation of resource-utilization variations over time in one or more sites. Furthermore, detailed analysis could be done in specific areas of treatment and care, and could facilitate investigation of the cost-effectiveness of alternative policy and care options

in these areas (for example, HIV screening and combination triple therapy). Finally, the SHCF could provide a starting point for further development of the approach to cover non-hospital care and social care. It could prove a useful basis for investigating the feasibility of applying general principles to other diseases, such as diabetes, cancer, lung and heart disease. This would enable valid comparisons of the intra-national and multinational cost impact of different diseases. However, ultimately the viability and usefulness of a standardised costing framework for HIV/AIDS care can only be fully tested through its application, in particular in the development of multi-national scenarios.

Chapter 8

Hospital Care for Persons with AIDS in the European Union

This chapter was published with the same title by MJ Postma, K Tolley, RM Leidl, AM Downs, EJ Beck, AM Tramarin, YA Flori, M Santin, F Antofianzas, H Kornarou, V Paparizos, MGW Dijkgraaf, JCC Borleffs, AHP Luijben, JC Jager for the European Research Team on AIDS Scenarios in *Health Policy* (1997, **41**:157-76);
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Abstract

This study estimates the current and future hospital resources for AIDS patients in the European Union (EU), using multi-national scenario analysis (EU Concerted Action BMH1-CT-941723). In collaboration with another EU-project ("Managing the Costs of HIV Infection"), six national European studies on the utilization of hospital care for AIDS have been selected to provide the data for our analysis. The selection criteria involve recentness, quality, comparability, accessibility and representativeness. Baseline hospital resource utilization is estimated for hospital inpatient days and outpatient contacts, using a standardized approach controlling for two severity stages of AIDS (chronic stage and late stage). The epidemiological part of the study is based on standard models for backcalculating HIV incidence and projecting AIDS incidence, prevalence and mortality. In the next step, baseline resource utilization is linked to epidemiological information in a mixed prevalence- and mortality-based approach. Several scenarios render different future epidemiological developments and hospital resource needs. For the year 1999 hospital bed needs of 10 000-12 700 in the EU are indicated, representing an increase of 20-60% compared to the estimated current (1995) level. The projected range for 1999 corresponds to a maximum of 0.65% of all hospital beds available in the EU. The growth in the number of outpatient hospital contacts is projected to possibly exceed that of inpatient days up to 1.82 million by the end of the century. Our methodology illustrates that estimation of current and future hospital care for AIDS has to be controlled for severity stages, to prevent biases. Further application of the multi-national approach is demonstrated through a what-if analysis of the potential impact of combination triple-therapy for HIV/AIDS. Estimation of the economic impact of other diseases could as well benefit from the severity-stages approach.

Context

This study has been performed for the European Research Team on AIDS Scenarios, that exists within the framework of the European Union Concerted Action on Multinational AIDS Scenarios (*project-leader*: Johannes C Jager PhD; *co-ordinator* economic aspects: Maarten J Postma MSc; BIOMED contract no PL941723). The co-operation with the other members of the co-ordinating team of the Concerted Action is kindly acknowledged: H Houweling MD (epidemiological aspects), SH Heisterkamp (modelling aspects) and DP Reinking MSc (social aspects).

8.1 Introduction

Several studies in the European Union (EU) have produced projections of the future costs of HIV/AIDS [213,270,295-298]. To date, such economic impact estimation has been limited to the level of an individual region or country. Only one study has attempted to go beyond the national level by developing several scenarios of the future bed needs and hospital costs for the EU as a whole [218]. Recently, an EU Concerted Action was initiated for the development of *multi-national* scenarios to estimate the epidemiological and socio-economic impacts of AIDS [107,111]. In this paper the impacts of AIDS on the hospital care systems are reported. Estimation of this impact at the multi-national level must be based on a standardized approach towards analyzing available national information on health-care resource utilization and costs, as has been developed in a parallel EU-project [66,95,96]. In addition, standardized surveillance and modelling of the national HIV/AIDS epidemics is needed, since the expected number of AIDS cases is the starting point of any estimation of the national burden on health-care resources [20,210].

Scenario analysis provides techniques for estimating disease impact under uncertain future conditions in terms of epidemiology, prevention, medical treatment and health-care technology. It involves the definition of a generic set of future projections, representing different "what-if" scenarios which are compared to a specifically defined baseline including the reference scenario [97]. Our previous analysis [218] suggested that hospital bed needs of persons with AIDS (PWAs) in 1995 would range from 5000 to 10 000 for the EU as a whole, based on reported average intensities of care in the few European studies on hospital resource utilization that were available at that time. It was impossible to specify the care intensities according to patient characteristics, such as severity level of AIDS. Since this time, more data have become available and further progress has been made in the methodology of multinational scenarios through the EU Concerted Action. In the present paper, methodological improvements in the scenarios on hospital care and updated multi-national scenario results are presented. In particular, an approach is applied that allows the specification of relevant stages of disease severity. The choice for an actual severity staging is related to differences in health-care utilization within the AIDS stage, between the AIDS stage and pre-AIDS stages and to effects of recently introduced new therapies to HIV/AIDS (for example, combination triple-therapy).

The next paragraph focusses on a standardized approach for comparing data from international databases on hospital resource utilization of PWAs, accounting for stages of

disease severity. Furthermore, the incorporation of severity stages in the projection/scenario methodology is described. As primary result a baseline set of scenarios is presented for hospital bed needs and outpatient hospital facilities by the end of the century for the EU, using a standardized model for the past, current and future development of national HIV/AIDS epidemics. Finally, a "what-if" analysis of the potential impact of combination triple therapy is presented and an application of our approach to other diseases is discussed. In general, this study can benefit the planning of hospital care facilities for PWAs in the next years at the EU-level.

8.2 Data and Methods

8.2.1 Backcalculation and Epidemiological Information

In the framework of a previous [108,141] and the current EU-Concerted Action an empirical backcalculation methodology has been developed and applied as a standard approach for epidemiological estimations in all European countries [299]. Our latest application [84] was based on AIDS surveillance data as of March 31st 1994 according to the 1987 AIDS surveillance case definition [7,8]. A staged model is used for disease progression [300] that takes into account under-reporting, delays in reporting [143] and possible effects of pre-AIDS treatments [301]. Work to improve and update the epidemiological model is still ongoing in the Concerted Action. Therefore the estimates used in this paper should be considered as preliminary.

For each individual EU member-state, the output of the epidemiological model comprises estimated (1978-1993) and projected (1994-1999) annual adult transmission-group-specific incidence of HIV and AIDS²⁵. In these calculations, two assumptions for the post-1993 HIV incidence were used to predict post-1993 AIDS incidence. In one, annual HIV incidence is constant from 1994 onwards at the estimated average 1990-1993 level. In the second *no new infections* occur after 1993, and thus provides an estimation of the unavoidable future AIDS epidemic given the prevailing treatment standards. Linking both assumptions with hospital care gives rise to respectively the Reference

²⁵ Because of small numbers the method was not applied to Luxembourg. In the present analysis we do not consider Luxembourg since the contribution to EU-totals on incidence, prevalence and health care-needs can be neglected. The three countries who joined the EU in 1995 (Austria, Finland and Sweden) are not yet included.

scenario (R) and the Unavoidable scenario (U). In the present analysis, prevalence and mortality of PWAs have been estimated from an assumed exponential survival distribution in the AIDS-stage with a mean of two years for PWAs diagnosed in 1987 or later, and one year for those diagnosed earlier [218]. In view of ongoing developments in AIDS therapies and related survival improvements [15,302], a third scenario is investigated labelled Therapy scenario (T). This scenario indicates the impact on prevalence and hospital care of prolonging survival to a mean of 3 years.

8.2.2 Information on Hospital Care in the EU: study selection

Several reviews summarize studies on the impact of AIDS on European health-care systems [109,110,303,304]. In addition, several new studies in this field have reported results in the last three years. In total 22 studies have reported results for hospital care utilization: one for Belgium [190], France [281] and Portugal [214], two for Germany [59,191] and Spain [193,295], three for Greece [192,282,283], Italy [65,284,285] and four for the Netherlands [62,220,270] and the UK [55,286,288,289]. Of the studies 50% refer to the 1980s, the rest include 1990 or later years. In general, sizes and distributions of the patient populations in these studies do not yet allow the assessment of differences between transmission groups. Inclusion of studies in this list is based on minimum technical standards on quality and comparability, related to the sample size, registration period and reporting (for example, of disease stage) [95].

For the present purpose of linking epidemiology and health care in future scenarios a further selection of studies was necessary. Three criteria were adopted. Firstly, information should be recent (1990 or later) reflecting current efficiency of practices in hospital care. During the 1980s and into the 1990s, efficiency has changed due to increasing experience with managing PWAs [221,305]. Furthermore, resource utilization has been controlled by more effective use; for example the substitution of less expensive outpatient care for hospital inpatient care [306]. Secondly, selected studies should include data that can be assumed to be representative of the national situations. Representativeness of study estimates is considered to be safeguarded in multi-center studies. Thirdly, the resource utilization data of selected studies should be *patient-based*, enabling resource utilization to be linked to individual patients, patient groups and disease stages, such as HIV infection and specific opportunistic illnesses. The studies satisfying most of these criteria are summarized in Table 8.1 [32,292,307-313].

Table 8.1 *Selected studies on hospital resource utilization for scenario analysis*

Country and reference	Period	Hospitals	PWAs	PY ^{CS}	PY ^{LS}
France [281,292,293,307]	1992-93	9	1384	922	237
Greece [282,283,308-310]	1990-91*	2	101	86	36
Italy [65,311]	1994	10	264	104	40
Netherlands [32,270]	1991-92	4	182	145	39
Spain [312]	1990-93	1	97	30	21
UK [286,313]	1990-91	1	122	67	25

The table includes the estimation period, number of hospitals involved, number of persons with AIDS (PWAs), number of person-years in the chronic stage (PY^{CS}) and the number of person-years in the late stage (PY^{LS}).

* In the Greek study some pre-1990 registration could not be excluded.

8.2.3. The Severity-Staging Concept

Several studies have indicated the importance of severity-of-illness for resource utilization of PWAs [277,278,314-317]. In some studies a U-shaped relationship between AIDS-related resource utilization and disease progression has been hypothesized [318-320]: high resource utilization immediately following the AIDS diagnosis and during the late terminal stage and low resource utilization during the intermediate period. This pattern describes the development of economically defined severity levels. Fig 8.1 presents information for hospital inpatient days using data from one Dutch study [320]. Clearly, the rise in resource-utilization intensity is more pronounced for the late phase and extends over several subperiods, whereas the rise in intensity after AIDS diagnosis seems to exist only in the first subperiod. Further analysis excluding PWAs with *Pneumocystis carinii* pneumonia (PCP) as AIDS-defining diagnosis, demonstrated intensities of hospital inpatient-days utilization below the average level in both the period following the onset of the disease and the intermediate phase (Fig 8.1). The availability of PCP prophylaxis in recent years supposedly contributed to "a shift in inpatient days utilization from the time near date of diagnosis toward the time of death" [321]. Compared to other periods, almost fourfold hospital inpatient resource-utilization or costs during the last half year of life is reported for the Netherlands and the USA in the early 1990s [270-273].

Fig 8.1

Mean number of inpatient days per person-year in the Academic Hospital Utrecht (Netherlands; [320]) for 11 consecutive subperiods during the AIDS-stage for all patients who died in 1990-92 (black bars; $n=54$; 43.28 person-days per subperiod) and excluding those with *Pneumocystis carinii* pneumonia (PCP) as AIDS-defining diagnosis (grey bars; $n=32$; 36.82 person-days per subperiod); lines indicate average levels for all patients (solid) and for non-PCP patients (dotted)

In consequence of the above, a study with a relatively large share of late-stage PWAs is likely to report a completely different pattern of hospital inpatient resource utilization than one with predominantly non-late stage (chronic) PWAs. Neglecting this phenomenon could lead to serious errors in estimating hospital resource-utilization parameters per person-year (ppy) [156,322]. Two stages for PWAs are therefore differentiated: a final stage of maximally 6 months before death (*late stage*; LS) and a stage for the foregoing period (*chronic stage*; CS). This staging concept has previously been applied to the Netherlands [270].

8.3.3 The Severity-Mix Modelling Approach

Standardized data on person-years, inpatient days and outpatient contacts (outpatient visits or day-care treatments) were collected from the selected studies, in order to estimate resource utilization ppy in CS and LS. Person-years and resource utilization were attributed to LS if they occurred during the final half year of AIDS preceding death²⁶

²⁶ If the period between AIDS diagnosis - or the start of the registration - and death was less than half a year, the whole period was attributed to LS.

and were attributed to CS if they occurred before the final 6 months preceding death (for deceased patients) or before the last 6 months of their registration (for patients alive by the end of the registration or follow-up period). The last column in Table 8.1 shows person-years in CS and LS in the selected studies.

In the next step epidemiological information was linked with ppy hospital resource needs of PWAs. Estimated ppy hospital resource utilization was used as a proxy for resource needs, implicitly assuming that recorded resource utilization reflects actual care needs. The approach adopted for linking was a mixed prevalence- and mortality-based approach. Annual resource needs for CS were estimated by multiplying the annual period-prevalence in CS by the appropriate ppy resource-need parameters for CS²⁷. Annual resource needs for LS were estimated by multiplying annual mortality by the duration of stay in LS (6 months or less) and the appropriate ppy resource-need parameters²⁸. It was assumed that ppy resource need remains stable over calendar time in each stage so that the effect of changes in epidemiology can be isolated. Estimates are presented for the years 1990, 1995 and 1999, using computer simulation and a spreadsheet. The year 1990 was chosen as the baseline year since epidemiological estimates are reliable and the economic data used are centered around 1990 in the original studies. The year 1995 was included to enable comparison with our previous estimates.

²⁷ Period-prevalence of PWAs was measured in terms of person-years. For simplicity, we modelled the AIDS incidence to occur halfway the year. The formula for the number of person-years in CS in year t , $PY^{CS}(t)$, is

$$(P(t)-I(t)*P[S>0.5])*1.0 + I(t)*P[S>1.0]*0.5 + I(t)*P[0.5<S<1.0]*E[S-0.5 | 0.5<S<1.0]$$

With $P(t)$ the end-of-the-year prevalence, $I(t)$ the incidence in year t , $P[S>0.5]$ is the probability of a PWA surviving longer than a half year after AIDS diagnosis, $P[S>1.0]$ is the probability of a PWA surviving longer than one year after AIDS diagnosis, $P[0.5<S<1.0]$ is the probability of a PWA surviving between a half and one year and $E[S-0.5 | 0.5<S<1.0]$ the expected survival in CS of PWAs surviving between a half and one year (slightly less than 0.25 years due to the characteristics of the exponential distribution). The factors 1.0 and 0.5 represent the durations of stay in CS of respectively the non-incident and the incident parts of end-of-the-year prevalence.

²⁸ The formula for the person-years in the late stage in year t , $PY^{LS}(t)$, is

$$(M(t)-P[S<0.5]*I(t))*0.5 + P[S<0.5]*I(t)*E[S | S<0.5]$$

With $M(t)$ mortality in year t , $P[S<0.5]$ reflects the probability of a PWA surviving less than a half year after AIDS diagnosis and $E[S | S<0.5]$ the expected survival of PWAs dying within a half year after AIDS diagnosis. The latter duration is smaller than 0.25 years due to the characteristics of the exponential distribution used. The factor 0.5 in the first part of the formula reflects the duration of stay in LS of PWAs surviving half a year or longer.

8.2.4 Generalization to the Whole EU

Table 8.1 provides a partial picture of AIDS hospital resource utilization patterns in the EU. No adequate hospital resource-utilization information could be selected for Ireland (no studies available), Belgium (most recent available study was from 1988), Denmark (most recent available study was from 1986) and Germany (most recent available study was from 1987) and Portugal (no patient-based information and no information on ambulatory hospital services available). To generalize our results to the whole EU, average ppy resource needs in CS and LS for each year in the countries of Table 8.1 were calculated, and applied to the countries with missing information. To indicate some of the sensitivity of the results with regard to this assumption, as an alternative data of neighboring countries were applied to the missing countries (Dutch data for Germany and Denmark; French data for Belgium; Spanish data for Portugal; UK-data for Ireland).

8.3 Results

Table 8.2 presents estimated hospital resource utilization per person-year for the two severity stages of PWAs. Inpatient days ppy vary between 4 (Greece; CS) and 160 (Spain; LS). Inpatient days ppy in the late stage are several times those in the chronic stage. In Greece relatively frequent use is made of outpatient services for CS patients (one of the two Greek hospitals specializes in dermatology, involving a high intensity of outpatient-care management). In both Italy and Greece total hospital contacts ppy are rather similar for CS and LS²⁹. France and Spain exhibit the opposite pattern of a high proportion of inpatient resource utilization (up to 93% for LS patients in France). Furthermore, in these two countries and the Netherlands and the UK total hospital contacts ppy exhibit greater care intensities for LS than for CS. Total hospital contacts ppy in CS are around 70-80 for France, Greece and Italy and around 35-45 for the Netherlands, Spain and UK. Estimated ppy outpatient contacts don't provide an obvious pattern: lower for CS than LS in Spain and the UK, similar in France and the Netherlands and higher for CS than LS in Greece and Italy.

The epidemiological results for the EU are used as a basis for estimating total current hospital resources for PWAs and producing future resource-needs scenarios. End-

²⁹ Total hospital contacts are the sum of inpatient days and outpatient contacts and represent the intensity of hospital-patient interaction.

of-the-year prevalence is estimated to have grown from 25 000 PWAs in 1990 to 49 000 in 1995 (Fig 8.2). Projections corresponding to the three scenarios all demonstrate a higher prevalence in the year 1999 (up to 86 000 PWAs for the therapy scenario T). The projection for the unavoidable scenario U - without new HIV infections since 1993 - shows an increase of 18% between 1995 and 1999. The reference scenario R - including new HIV infections from 1994 onwards - indicates an increase of 27% over the same period. Due to the fact that AIDS incidence is higher than AIDS mortality, the estimates of person-years (Fig 8.2) are below estimated prevalences (end-of-the year prevalence includes incident cases and neglects mortality). The severity mix is such that 22% of the person-years refers to LS, except in scenario T where only 15% refers to LS. The North-South shift in the AIDS epidemic causes the proportion of person-years in Spain and Italy in the EU-total to increase from 42% in 1990 to 56% in 1999.

Table 8.2 *Hospital resource utilization per person-year of AIDS by country and patient group (chronic versus late; see text)*

Country	AIDS stage	Inpatient days	Outpatient contacts	Total contacts
France	Chronic	57.2	12.7	69.9
	Late	143.4	11.0	154.4
Greece	Chronic	4.3	75.6	79.9
	Late	44.1	33.8	77.9
Italy*	Chronic	32.6	44.1	76.7
	Late	59.8	28.5	88.3
Netherlands	Chronic	23.5	21.0	44.5
	Late	79.7	22.9	102.6
Spain®	Chronic	22.6	13.6	36.2
	Late	159.8	22.9	182.7
UK	Chronic	26.8	14.9	41.7
	Late	65.1	22.8	87.9

* Due to the relatively short registration period of 7 months, the last 6 months before registration closure of surviving patients were not discarded, which would have left only one month per surviving patient; instead, all person-years and resource utilization of patients with a relatively short life expectancy were attributed to LS, in particular of those diagnosed in the most severe Turner-stage with an estimated median survival of 7 months [277,278]; the Italian database is the only selected database that includes information on the Turner-stages; ® Since the registration is based on episodes of disease, the last half year had to be approximated by taking the last or last few episodes.

Sources: as in Table 8.1.

Fig 8.2

AIDS prevalence (black bars) and person-years in 1990, 1995 and three scenarios for 1999 (R, U and T: see text); person-years are differentiated between chronic stage (CS; grey bars) and late stage (LS; white stacked bars)

Fig 8.3

Hospital bed needs (left bars; left axis) and outpatient contacts (right bars; right axis) for AIDS in 1990, 1995 and three scenarios for 1999 (R, U and T: see text); contributions to resource needs are differentiated between chronic stage (CS; black bars: beds; dark grey: outpatient contacts) and late stage (LS; light grey stacked bars: beds; white: outpatient contacts)

In the reference scenario, hospital bed need is projected to increase by 28% from 8100 in 1995 to 10 400 in 1999 (Figure 8.3)³⁰. Respective growth rates for scenarios U and T are 22% and 57%. The latter growth rate for scenario T indicates that person-years outgrow hospital beds by 13%. The corresponding projected trend in ppy inpatient days is therefore downward in scenario T, as opposed to the stabilization projected in scenarios R and U (1990: 54.5; 1995: 53.7; 1999R: 53.3; 1999U: 53.4; 1999T: 47.4). The trend in this "average EU ppy inpatient-days figure" is affected by two driving forces: the distributions of person-years (1) over countries (geographical development) and (2) over CS and LS (severity-mix development). The increasing relative importance of the Spanish and Italian epidemics in the EU causes a downward pressure on total EU ppy inpatient days due to the relatively low ppy inpatient days for CS in Spain and LS in Italy. Reductions in overall ppy inpatient days for scenarios R and U can be explained by the dominance of the geographical development. The severity-mix development dominates scenario T, where the explicit assumption of increasing survival inflates the relative importance of CS with relatively low ppy inpatient days. Ppy inpatient days for CS and for LS are respectively 34-37 and 118-119. Except for scenario T, there exists a tendency of a growing contribution of LS to EU bed needs, towards 50% in 1999. Because the intensity-of-care in terms of nursing, specialist consultations and drugs is probably higher for PWAs in LS, the average inpatient day in 1999 carries a higher burden-of-care. As an important consequence, in two of the scenarios a higher average burden-of-care per inpatient day adds to the projected growth in the number of inpatient days.

In the reference scenario, hospital outpatient contacts are projected to increase from 1.0 million in 1995 to 1.3 million in 1999 (Fig 8.3). Respective growth rates for scenarios U and T are 22% and 78%. For all scenarios, growth rates are identical to those for total person-years. Therefore, corresponding projected ppy outpatient contacts are stable over time and between scenarios with a range from 20.9 in 1990 to 21.8 in later years. The increase from 1990 onwards can be explained by the increasing importance of the Italian epidemic in the total EU-epidemic, with relatively high ppy outpatient contacts in Italy. Ppy outpatient needs differ little between CS and LS (respectively 22 versus 21). As for person-years, approximately 80% (85% in scenario T) of outpatient contacts are associated with CS. In general, the share of outpatient contacts in total hospital contacts is projected to increase slightly from 29% of 3.5 million contacts

³⁰ Scenarios on bed needs are derived from the inpatient days estimates, assuming a bed-occupancy rate of 85%.

in 1995 to up to 31% of 5.8 million contacts in scenario T in 1999.

8.4 Discussion and Conclusions

8.4.1 The Severity-mix Approach

To make relevant comparisons and projections, resource utilization studies have to be standardized with respect to the severity mix of the patient population. Neglecting the severity mix would overestimate resource utilization of the "average PWA" in a study with a relative high proportion of severe patients. As mentioned above, our severity-weighted EU-average in 1990 for ppy inpatient days amounts to 54.5. Its unweighted counterpart would be 62.6 ppy inpatient days in that same year, illustrating the importance to account for severity mix. Our operationalization of the severity concept in chronic and late stages (CS and LS) has been chosen in accordance with major European resource-utilization studies and with the outcomes of epidemiological modelling. The estimates demonstrate a significantly higher ppy inpatient-day utilization in LS than in CS. Our findings on the relatively high resource utilization in the late stage of AIDS resemble results of US-studies on health-care resource utilization in the late stage of any disease [323-326]. In 1961 it was assessed that hospitalization costs of adults who died in that year were 3 times those of survivors [327]. Lubitz and Prihoda [328] found that 5.9% of Medicare insured (primarily elderly) patients who died in 1978 accounted for 27.8% of total Medicare expenditures. In general, ppy costs in the final year of life are 6.8 times those for patients who were alive at the end of the year, ranging from 5.2 to 10.3 times depending on the underlying cause of death [290,291,329]. Hospital inpatient days ppy exhibit a similar factor of 6.8 on average. Up to 80% of costs in the final year of life appear in the final 6 months of life (for example, in 1988 ppy Medicare expenditures in the last half year of life were 11.1 times ppy expenditures excluding the last 6 months). Therefore, severity staging as applied to AIDS is probably relevant to other diseases as well. Furthermore, our severity-staging can easily be extended to other diseases since it is relatively straightforward, based on time distance to the point of death.

Several studies have registered decreasing trends in ppy hospital inpatient days [220,286,289]. It has been shown that an important factor for explaining these trends is a shift in the severity-mix in favor of CS if survival increases. Extending our model backwards gives ppy inpatient days for the pre-1990 period, as an example the year 1986

is elaborated here (Fig 8.4). In 1986 the patient group with one year average survival dominated and ppy inpatient days is estimated at 67 for the EU as a whole. Fig 8.4 reflects modelled response of ppy inpatient days to an ongoing increase in survival from 1 year in 1986, 2 years in 1995 to three years in 1999 in scenario T. The country-specific results of our severity-staging model are in line with the reported trends in the Netherlands and the UK [220,286,289]. Similar mechanisms can be assumed for other countries as well (Spanish results are shown in Fig 8.4 as well).

Fig 8.4 *Model-based trends in hospital inpatient days per person-year: back-projected (1986), estimated (1995) and projected (1999) in scenario T (see text) for three countries and the EU as a whole*

8.4.2 Comparative Analysis

To compare the scenarios in this paper with our previously published projections [218], our current estimate of 54.5 ppy inpatient days in the EU in 1990 is substituted into the previous methodology. This would have produced a bed need of 3700 in 1990 and projections for 1995 ranging from 3800 to 5000. Our current estimates for those years are slightly higher for 1990 (3900) and significantly higher for 1995 (8200). Our previous approach to estimating person-years was based on the assumption that each AIDS case prevalent at the end of the year accounts for the whole of the respective year. Our current approach involves specific estimates of person-years for incident patients, patients who were prevalent during the whole year and for mortality. In addition, the correction for under-reporting of AIDS cases was undertaken for the current scenarios only, increasing the estimated prevalence by 18.5% for the whole EU in 1990 and 1995. These two

factors together can explain the slight increase for 1990. The major explanation for the significant difference in 1995 is a drastic change in epidemiological projection, previously showing a decrease in AIDS incidence to a low level in 1994 and 1995. Based on more recent AIDS incidence data [84], our current estimate shows an increasing or levelling AIDS incidence in the period 1990-1995, corresponding to a current AIDS prevalence estimate for 1995 of 48 500. This is 66% higher than the maximum estimate (29 300) in [218]. Obviously, there are still several factors causing under-estimation of the future health-care impact. The recent (1993) extension of the AIDS case definition to include pulmonary tuberculosis will increase the number of new AIDS cases. Furthermore, resource needs for pre-AIDS stages were not included, which might become more important if prophylactic treatment preventing the onset of AIDS becomes increasingly effective. Though the AIDS stage is certainly the most resource-demanding stage, further work should include multi-national research into resource needs of pre-AIDS stages.

In three scenarios hospital bed needs in 1999 are projected to increase by up to 57% compared to 1995. This corresponds to 0.40% in 1995 and up to 0.65% in 1999 of all EU-beds currently available [330]. Even in scenario U, reflecting the unavoidable future burden of AIDS on hospital care in 1999, a growth in hospital care needs of over 20% is indicated compared to 1995. Associated to survival improvements, the share of outpatient contacts in total hospital contacts is projected to rise from 28% to 31% in scenario T. The validity of such results is significantly extended by the severity staging used in this paper. Employment of this concept enables dynamic modelling of important model parameters, such as ppy inpatient days. Time-distance to the point of death has been used as the severity indicator. The relevance of this indicator for health care utilization and costs has long been recognized in the analysis of patient-based data across all diseases [290,291,323-329]. It has been used here to analyze the impacts of one specific disease on the health care systems. The indicator can obviously only be measured ex-post, and cannot be used to stage individual, living patients. In the scenario analysis presented, the ex-post measurement proved to be useful and feasible, because historical data on resource utilization developments preceding death were available for individual patients, and because future AIDS prevalences and mortalities could be described by an epidemiological model.

8.4.3 Further Application of the Multi-national AIDS-model

Our method involves the extrapolation of average results for France, Greece, Italy, Netherlands, Spain and the UK to Belgium, Denmark, Germany, Ireland and Portugal. One could question the representativeness of our selected countries for the rest of the EU. The share in total person-years of the six EU-countries included in the scenario analysis is 84% of the whole EU in 1990, with an expected increase to 89% in 1999. The potential impact on the whole EU of the countries without resource utilization information is therefore only limited. For the "unknown" part of the EU, Germany constitutes 50-75% of the person-years of AIDS. As an alternative the situation where ppy hospital resource-need parameters in LS and CS applied to neighboring countries is considered. Generally, this lowers the resource needs by approximately 10% in 1990, 6% in 1995 and 4% in 1999 for both hospital beds and outpatient contacts. The decrease of this percentage in time supports the robustness of our EU scenarios based on data from six countries. In two of these six countries data were available from one hospital only to describe the national situation. As has been shown for France [292] great differences between hospitals exist, implying that our estimates for Spain and the UK might not be representative. Further research involving more hospitals, is needed in these countries. Therefore, one should conceive the absolute level of our scenario results with great caution.

Our baseline set of three scenarios projects the future course of hospital care needs based on the most recent analyses of survival patterns and standardized multinational information on resource utilization. Recently, preliminary evaluations of new antiretroviral combination triple-therapy have given rise to speculations on drastic improvements of survival and corresponding prolongation of the chronic stages of HIV/AIDS [11]. The actual effect on survival is as yet highly uncertain and the effectiveness will depend on other factors, such as the acceptance, availability, patient and doctor compliance and costs of the new therapy. In particular, the costs are considered to be relatively high - approximately 15 000 ECUs per year of combination triple-therapy. However, significant cuts in HIV/AIDS hospitalizations in consequence of the new therapy have been suggested [331] and might impact on hospital resource needs for HIV/AIDS in the EU. This impact will involve structural effects due to increases in HIV/AIDS prevalence and transient effects due to the sudden introduction of the new therapy. In particular, a transient drop in hospital resource needs might currently take place because of the delay in progression to the resource-intensive late stage of AIDS. A similar phenomenon was previously observed when pre-AIDS AZT/zidovudine treatment

was introduced in the early 1990s [92]. At the moment the standardized information to estimate the full impact on resource utilization patterns and costs is lacking, in particular at the multinational EU-level. As our scenario analytic design specifies the relevant parameters involved in the impact of the new therapy, it does provide the setting for a what-if investigating into this impact on the short-term. Table 8.3 shows a range for the change in hospital bed needs in 1999, assuming extensions of HIV/AIDS survival due to combination triple-therapy of 3 and 5 years. As a first variant, ppy inpatient days estimates for the chronic AIDS stage (CS) are used for the years gained by the new therapy. As chronic-AIDS-stage's figures might not be representative lower levels of ppy inpatient days are included, in line with reported levels for pre-AIDS stages [95]. Tabulated calculations suggest that a larger number of patients will be alive and in treatment than the reference scenario indicates, bed needs vary between levels of plus 15% and minus 35% of the reference scenario. Momentarily, these indicative results are investigated in depth by using the French and UK databases [286,292]. As assessments of the cost-effectiveness of new therapies is becoming more and more the vogue [31], our reference scenario is crucial in providing the point of departure to measure the impact of the new combination triple-therapy.

Table 8.3 *Potential consequences of combination triple therapy in 1999: percentage changes in HIV/AIDS prevalence and bed needs compared to the reference scenario*

Survival increase Inpatient-day needs	3 years			5 years		
	100%	50%	25%	100%	50%	25%
Prevalence	+50%	id	id	+69%	id	id
Bed needs	+14%	-15%	-30%	+18%	-19%	-37%

Different assumptions refer to therapy-related increases in HIV/AIDS survival of 3 and 5 years with inpatient-day needs similar (100%) to those in the chronic AIDS stage or lower (50 and 25%).

The scenarios on the health-care impact of AIDS presented provide information that can be used to support health-policy decisions in the field of AIDS. First, scenario results give an order of magnitude of future health-care needs in terms of total hospital beds, outpatient contacts and the patient-mix to be cared for. In addition to hospital capacity planning, the multi-national EU-scenarios also provide background information for the further planning of EU AIDS research and prevention programs. At the national level and even at lower levels, the scenarios provide an indication of the change in

severity-mix that can be expected within total hospital need for AIDS patients, which under certain circumstances has been shown to vary significantly and which can pose new management tasks. International comparison has further made clear that future analyses, either at the national or at lower levels, must account for severity-mix in order to avoid bias in any projections. Future research work could further refine the staging-mechanism in case of AIDS, and would certainly require to continue, extend and validate the national databases used. This paper has presented scenario information for health policy making at the EU-level and at the national levels on the case of AIDS. It is also obvious that comparable information on other diseases which are in the special focus of EU policy, such as cardiovascular diseases and cancer, is lagging behind as compared to the information now available for AIDS.

Chapter 9

Hospital Care for Persons with AIDS in European Union Countries; a cross-country comparison

This chapter is based on **Hospital Care for Persons with AIDS in Greece and the Netherlands; assessment of current and future impact** by MJ Postma, H Kornarou, V Paparizos, R Leidl, K Tolley, J Kyriopoulos, JC Jager for the European Research Team on AIDS Scenarios *in: J Kyriopoulos *et al.* (Eds) AIDS Cost Analysis and Patient Classification* (in press)

Abstract

This paper investigates AIDS hospital care in selected European Union (EU) countries. In particular, hospital resource utilization in multi-hospital registrations in France, Greece, Italy, the Netherlands, Spain and France is analyzed. Baseline hospital resource utilization is estimated for hospital inpatient days and outpatient contacts, using a standardized approach controlling for severity stages of AIDS. These estimations are linked to standard models for epidemiological estimation and projection, in an incidence-based approach. Respective estimations are compared between countries and related to characteristics of the national HIV/AIDS epidemics and health care systems. These country-specific results are underlying a set of projections for the EU as a whole (published elsewhere previously).

A person with AIDS (PWA) has some kind of contact - inpatient day or outpatient visit - with the hospital in 14% (UK) to 24% (France) spend in the AIDS stage. Estimated hospital bed needs for AIDS in 1995 are up to 2.13% (Spain) of total national acute-care hospital beds available. Estimated per-capita needs for outpatient visits in 1995 are highest in Italy, corresponding 108 doctor full-time equivalents. In line with per-capita epidemiological impact, per-capita hospital resource needs for AIDS are limited in the Netherlands and the UK.

For Greece and the Netherlands, differences in hospital resource utilization patterns are in line with differences between both health care systems (number of hospital beds, doctors and nurses per capita and some qualitative characteristics of medical care in both countries). In general, international comparison of AIDS hospital care is possible using standardized data analysis of national hospital resource utilization studies and standardized epidemiological modelling.

Context

This study has been performed for the European Research Team on AIDS Scenarios, that exists within the framework of the European Union Concerted Action on "Multi-national AIDS Scenarios" (*project-leader*: Johannes C Jager PhD; *co-ordinator* economic aspects: Maarten J Postma MSc). The study has been performed in the framework of this Concerted Action (BIOMED contract no PL941723) and the European Union Project on "AIDS Cost Analysis and Patient Classification" (*project-leader*: Prof John E Kyriopoulos). SH Heisterkamp PhD is acknowledged for statistical advice.

9.1 Introduction

In 1993, a European Union (EU) Concerted Action of the Biomedical and Health Research programme started for the development of *multi*-national assessment of the epidemiological, economical and social impacts of AIDS on society [111]. The participants in the EU-CA represent expertise in the fields of modelling, statistics and operations research, surveillance and epidemiology, health economics and health-services research, social sciences and scenario analysis; furthermore they represent most EU-countries. The standardized approach of analyzing available national information on health-care resource utilization, as has been developed in a parallel EU-project [66], is the starting point for the economic impact assessment in the EU-countries. In addition, standardized surveillance and modelling of the national HIV/AIDS epidemics is needed, since epidemiology is the focus of any assessment of the national burden on health care resources [210]. Much work has been done in this field in the past years, and the development of advanced standardized methods is progressing [20].

Country-specific results have been aggregated to a multi-national economic impact assessment for the EU as a whole [114]. For example, we showed that AIDS hospital inpatient care involves an estimated 0.40% of all available inpatient beds in the EU. Underlying this multi-national estimate of EU-totals for current hospital-care needs are country-specific estimates for the majority of the EU-countries. In this paper results from selected databases on AIDS hospital care in six European countries are presented. These databases were selected out of a total of almost 30 studies on hospital care in European countries. Elaborating on these data, this paper addresses the direct comparison of AIDS care in six EU-countries. The standardized approach chosen to work with these data enables valid comparisons to be made of hospital care for persons with AIDS (PWAs) between countries. The first part of this study presents these type of results on hospital inpatient days and ambulatory hospital care for six EU-countries (France, Greece, Italy, Netherlands, Spain and UK).

Furthermore, the standardized approach allows the identification of "real factors" of health-care systems determining AIDS care, such as the number of hospital beds, occupancy rates, numbers of doctors and nurses and organization of inpatient/outpatient care. Therefore, the second part of this study, addresses a selected comparison of AIDS care in two countries. As a comparison was previously made for Greece and the Netherlands in the context of the EU-project on "AIDS Cost Analysis and Patient Classification" (co-ordinate at the National School of Public Health, Athens Greece),

these two countries are chosen. Also, Greece and the Netherlands have similar AIDS epidemics on several aspects (PWAs per capita, predominantly homosexual patient population), whereas health-care systems differ on various aspects. In consequence - in a quasi-experimental design - we study rather similar epidemics in different health-care systems.

9.2 Data

In the framework of a previous [108] and the current EU Concerted Actions (*see above*) a methodology was developed and applied as a standard approach for epidemiological estimations in all European countries. AIDS surveillance data of the European Centre for the Epidemiological Monitoring of AIDS (Paris) as of March 31th 1994 according to the 1987 AIDS surveillance case definition were used as an input for this approach [84]. To calculate AIDS survival an exponential distribution with a mean survival of two years in the AIDS stage was used [14].

National studies were selected for extracting relevant information on hospital care. Studies are selected according to specific criteria. Since studies that extend over several years show a decreasing trend in per person-year hospital inpatient days utilization [220,289] a first criterium for selecting information for scenario analysis was *recentness*. Secondly, they should include data that can be supposed to be reasonably representative of the national situations. Therefore, preferably information should come from *multi-hospital* studies. Thirdly, the resource utilization registration of selected studies should be *patient-based*, enabling linkage of resource utilization to individual patients and patient groups according to, for example, illness, severity and health status. The studies satisfying most of these criteria are summarized in Table 9.1. Utilization figures refer to the period 1990-94. Baseline hospital services utilization was estimated for inpatient days and outpatient contacts (outpatient visits and day-care days).

Cross-country Comparison

Table 9.1 *Selected studies on hospital resource utilization: country, references, estimation period, number of hospitals involved and number of persons with AIDS (PWAs) in the study (Source: [114])*

Country and reference	Period	Hospitals	PWAs
France [281,292,293,307]	1992-13	9	1384
Greece [282,283,308-310]	1990-91	2	101
Italy [65,311]	1994	10	264
The Netherlands [32,270]	1991-92	4	182
Spain [312]	1990-93	1	97
UK [286,313]	1990-91	1	122

Baseline hospital care utilization was expressed per person-year and severity stage. Previously for the Netherlands, we have developed a further staging of the AIDS-stage into a possibly long chronic (early) substage and a short (maximally a half year) late terminal substage [270]. This staging is relevant to account of differences in severity of illness. Intensity of hospital inpatient days utilization in the late stage appeared to be almost four times that in the chronic stage. Furthermore, more than half of the lifetime hospitalization costs are generated during this final half year in the late stage. Similar findings are reported in the the American literature [271-273]. For example, one study shows that hospitalization costs in 1990-91 for PWAs rise sharply in the final six months prior to death up to \$ 23 000, compared to below \$ 7000 in other sixmonthly periods [273]. For outpatient hospital costs, the US study shows a slight drop in the late stage of AIDS, which is in line with a relatively high involvement of inpatient care in terminal care.

In consequence of this, studies with completely different distributions over late and non-late (chronic) stages of PWAs are likely to report completely different ppy hospital inpatient resource utilization. Neglecting this phenomenon could lead to serious errors and biases in estimating hospital resource utilization and hence in scenario analytic projections [322]. We have therefore chosen to adopt the further staging of AIDS in this paper as well. In the progression-of-disease model for the AIDS-stage we differ between a period lasting for a maximum of a half year before death (*late stage*; LS) and the foregoing period (*chronic stage*; CS). Estimated ppy hospital resource utilization is used as a proxy for resource needs, implicitly assuming that recorded resource utilization reflects the actual care needs.

9.3 Methods

An incidence-based approach was applied to derive lifetime person-years in the AIDS stage and to link epidemiologic and hospital-care data. Illustrating this approach, lifetime hospital inpatient-day needs can be derived from our estimates of per person-year (ppy) resource needs in the chronic stage (CS) and late stage (LS) - respectively $ppyIPD^{CS}$ and $ppyIPD^{LS}$. If λ reflects the parameter of the exponential distribution for AIDS survival it can be proved that the expected value of the lifetime number of inpatient days is

$$\exp(-\lambda/2)/\lambda * ppyIPD^{CS} + ((1-\exp(-\lambda/2))/\lambda) * ppyIPD^{LS}.$$

The formula expresses that the expected durations in both chronic and late AIDS stages are multiplied with the appropriate ppy inpatient-days needs. As mentioned, in this study results were evaluated for a total survival in both AIDS stages of $(1/\lambda =) 2$ years.

In the next step, lifetime hospital resource needs of PWAs are linked to estimated AIDS incidence for 1995. The incidence-based approach used for estimating hospital care impact involves a straightforward multiplication of annual incidence and lifetime resource needs. In this paper hospital resource needs are evaluated on the basis of AIDS incidence; an alternative would be to use HIV as a starting point. The incidence-based approach doesn't show actual annual burdens of care, it is favoured in situations where all resource needs associated with the incidence of the base-year are to be expressed.

The two-stage-model (CS and LS) introduces statistical variability in resource needs. Let:

$$D^{LS} = T \text{ and } D^{CS} = 0 \quad \text{if } T \leq 0.5 \text{ years}$$

$$D^{LS} = 0.5 \text{ and } D^{CS} \neq 0 \quad \text{if } T > 0.5 \text{ years.}$$

D^{LS} and D^{CS} reflect durations of stay in respectively late and chronic stages. Associated variance for lifetime inpatient days is:

$$\text{Var}(D^{CS}) * (ppyIPD^{CS})^2 + \text{Var}(D^{LS}) * (ppyIPD^{LS})^2 + 2 * \text{Cov}(D^{CS}, D^{LS}) * ppyIPD^{CS} * ppyIPD^{LS}.$$

Here, $\text{Var}(D^{CS})$ and $\text{Var}(D^{LS})$ reflect the variances of durations of stay in LS and CS and

$\text{Cov}(D^{CS}, D^{LS})$ reflects the covariance of both durations of stay³¹:

$$\text{Var}(D^{CS}) = (2 * \exp(-\lambda/2) - \exp(-\lambda)) / \lambda^2;$$

$$\text{Var}(D^{LS}) = (1 - \exp(-\lambda) - \lambda * \exp(-\lambda/2)) / \lambda^2;$$

$$\text{Cov}(D^{CS}, D^{LS}) = ((0.5 * \lambda - 1) * \exp(-\lambda/2) + \exp(-\lambda)) / \lambda^2.$$

Confidence intervals for hospital inpatient-day needs of a cohort of incident PWAs result from applying the Central Limit Theorem. An example is presented in chapter 8 for the Netherlands [322]. Such confidence limits are elaborated for a range of 1995-incidences of PWAs (normality assumption on ranges reported in [84]). For example, the 95%-confidence limit for French incident PWAs in 1995 is 6193-7684. Finally, 95%-confidence limits are approximated for country-specific total hospital inpatient-day needs³².

To allow valid comparisons between countries and with EU-averages, hospital resource needs are presented per million population [332]³³.

9.4 Results at the EU-level

Figure 9.1 shows country-specific expected lifetime hospital resources for a PWA during the expected two years survival in the AIDS stage. Italy, the Netherlands and the UK have comparable inpatient-days amounts of 70-80 on a lifetime basis. In Italy however, inpatient days reflect the minority of total lifetime hospital contacts, whereas in the other two countries outpatient involvement is below 40% in the total number of hospital contacts. In Greece the share of outpatient care is even above 80%. The lowest shares of outpatient care are found in France and Spain. All countries are similar in showing up a low outpatient involvement in the late stage of AIDS; Greece has a rather low hospital involvement in LS in general. The distribution of lifetime inpatient days over chronic and

³¹ The variance-formulas follow straightforward using the general relationship between the expectancy and variance of a variable X ($E[X]$ and $\text{Var}[X]$, respectively):
 $\text{Var}[X] = E[X^2] - E[X]^2$.

³² Similarly, 95%-confidence limits for lifetime AIDS person-years and outpatient-contact needs are derived.

³³ Inpatient days are transformed to hospital beds using an occupancy rate 85% [114].

late AIDS stages is approximately fifty-fifty for all countries, despite the relatively short duration of the latter stage (an expected 0.44 years in the late stage compared to an expected 1.56 in the chronic stage).

Fig 9.1 *Expected lifetime hospital resources for a PWA in six European countries: inpatient days in the chronic stage (black) and late stage (dark-grey); outpatient contacts in the chronic stage (light-grey) and late stage (white); the sum of inpatient days and outpatient contacts reflect total hospital contacts and represents the intensity of hospital-patient interaction*

The assumptions indicate that an incident PWA has some kind of contact - an inpatient day or an outpatient contact - with the hospital in 14% (UK) to 24% (France) of the days spent in the AIDS stage. These percentages are around the estimated EU-average of 20% for the incident PWAs in 1995 [114].

Hospital bed needs for 1995-incident PWAs range from almost 80 per million population in the upper 95%-confidence limit in Spain to only a few in Greece (Fig 9.2; left axis). Rankings of countries are generally in line with epidemiological impact; for example, both countries showing the highest hospital bed needs per million population (Spain and France) also have the highest estimated lifetime person-years per million population related to 1995-incident PWAs (95%-confidence intervals are 366-462 and 213-258, respectively). Contradicting epidemiological impact are Italian and Greek estimates. Italian hospital bed needs are less than half of the French, whereas lifetime person-years per million population almost similar (95%-confidence interval for lifetime person-years of 197-246); Greek hospital bed needs are disproportionate small compared to its epidemic (95%-confidence interval 28.9-60.5). Furthermore, Italian and Greek outpatient

contacts are higher than expected on the basis of epidemiological impact (Fig 9.2; right axis). Expressed in rankings, outpatient contacts in Italy are in first rank, whereas lifetime AIDS person-years rank after Spain and France; outpatient contacts in Greece rank third - only surpassed by Italy and Spain -, whereas lifetime AIDS person-years rank last.

Fig 9.2 *Hospital beds (left bars; left axis) and outpatient contacts per million population (right bars; right axis): expected values (grey), lower (black) and upper (white) 95%-confidence limits*

Summarizing, Italy and Greece seem to have relatively low bed needs and high needs for outpatient involvement. Hospital resource-need patterns in the other countries are in accordance with what would be expected from epidemiological impact. For example, we note a high similarity in Dutch and UK resource-need patterns, corresponding to a similarity in lifetime AIDS person-years per million population of 1995-incident PWAs (confidence intervals are respectively 51.6-82.8 and 60.1-84.7).

9.5 Comparing AIDS Care in two Selected Countries

This section illustrates AIDS hospital care in Greece and the Netherlands. These countries have quantitatively comparable AIDS epidemics (limited for EU-standards) and similar types of epidemics with the majority of AIDS-cases coming from the homosexual risk-group, with approximately 25% of the cases attributed to other transmission groups than the homosexual group in both countries [84]. Therefore, we can elaborate upon the developments of two comparable AIDS epidemics in two very different health-care

systems. The Greek system resembles the UK National Health Service in covering and financing health care costs. Hospital care is provided through public and private (33%) hospitals, with the latter type involving high co-payment, shorter stays and higher quality of care. The Dutch health care insurance is a mixed system of social and private health insurance funds. Finally, the Dutch have a much higher density of inpatient care beds per capita than the Greek have [333,334]. In fact, both studies provide a quasi experimental design for comparing hospital care utilization in two different health-care systems.

As shown (Fig 9.1), lifetime hospital inpatient days are significantly higher in the Netherlands, than in Greece, whereas outpatient contacts exhibit the opposite pattern. Referring to the quasi-experimental design underlying these figures and the standardized approach in calculating them, we could speculate on and analyze the differences between both countries. In general, differences in hospital management of PWAs between both countries may be related to factors associated with the health-care systems and with factors of epidemiological nature. To start with the latter, 60 of the 101 PWAs in the Greek hospital database are visitors of the hospital specialized in dermatology. Almost all of these visitors are homosexual men with a high occurrence of complaints and treatment related to Kaposi's sarcoma (KS). The treatment of KS has a relatively high outpatient involvement with drug administering, blood testing and transfusion. PWAs treated for *Pneumocystis carinii* pneumonia (PCP) in this hospital had 110 outpatient contacts ppy, versus 150 for PWAs treated for other - primarily KS - conditions. Furthermore, inpatient days show the opposite pattern: 99.9 days ppy for PWAs treated for PCP and 22.3 for non-PCP PWAs. So, AIDS manifestation form influences results.

The most striking difference between hospital-care systems in Greece and the Netherlands concerns the number of inpatient beds per capita; the Dutch level more than doubles that of Greece - approximately 11.5 versus 5.1 in 1990 [335]. Although the Greek multi-hospital study refers to the Athens region (Attica) with a 15% higher bed density than average [336], this difference could be one of the explanations for the lower ppy inpatient-days utilization for AIDS in Greece. Furthermore, the Greek system has a large share of the private for-profit sector in the provision of hospital care, whereas in most other EU-countries - for example, the Netherlands - all hospital beds are not for profit. In Greece, approximately one third of the hospital beds belong to the for-profit sector, leaving only 2.7 public not-for-profit hospital beds per 1000 population. The high co-payment required in private hospitals, together with high quality and comfort in these hospitals have caused great inequalities and accessibility problems in hospital care [337]. In particular the latter, might also have contributed to low inpatient hospital utilization

compared to other EU-countries.

The relative scarcity of nurses in Greece (approximately 2 per 1000 population versus 6.0 in the Netherlands) and the low occupancy rate of hospital beds (Greece 55-65%; the Netherlands 73%) are also in line with low levels of inpatient hospital care utilization for AIDS in Greece compared to the whole EU-spectrum, and the Netherlands in particular [338-340]. However, Greece has one of the highest number of doctors in the EU (approximately 3.5 per 1000 population versus 2.2 in the Netherlands), which is a possible factor for high levels of hospital outpatient care [341]. Whereas in the Netherlands the General Practitioner is the "gatekeeper" to hospital care almost all Greek doctors are specialists and a "gatekeeper" is lacking [335]. A programme to develop primary health centres was executed in the 1980s in rural areas, but the plan to build urban centres was postponed and the outpatient facilities of public hospitals are still performing the primary care in urban centres, such as Athens. As a consequence, doctors in urban outpatient facilities see many patients with sometimes only a very short visit for, for example, prescribing drugs only [342-345]. These features of the Greek and Dutch systems are in accordance with a higher outpatient share in total hospital care in Greece.

9.6 Discussion and Conclusions

Table 9.2 shows expected hospital bed needs represented as percentages of national total acute care hospital beds available. This percentage ranges from 0.05% (Greece) to 2.13% (Spain). In terms of inpatient care AIDS is estimated to have posed a significant managerial challenge to Spanish hospitals. Also for France, a share of AIDS care in inpatient hospital care of more than one percent is estimated. Italy comes up with a share of only a half percent. On the other hand an estimated 108 full-time equivalents of specialists³⁴ are needed to provide the outpatient hospital care for Italian AIDS patients. Italian specialist time for outpatient hospital care represents half of estimated specialist time for outpatient care in the six selected countries together (222 full-time equivalents³⁴).

The importance of severity stages for AIDS have been pointed out previously for survival, costs and prospective financing [118,314,316]. Our operationalization of the concept of severity in chronic and late stages (CS and LS) has been chosen to suit the

³⁴ Based on an assumed duration of an outpatient hospital contact of 20 minutes and 200 working days per year for one full-time equivalent.

Table 9.2 *AIDS hospital bed needs in 1995 as percentage of national total numbers of acute care hospital beds available [45]*

France	1.26%
Greece	0.05%
Italy	0.51%
The Netherlands	0.19%
Spain	2.13%
UK	0.40%

outcomes of epidemiological modelling and to be in line with resource-utilization studies that have been set up in six EU-countries. We have previously shown the importance of AIDS severity stages for analysing AIDS resource-utilization databases and for constructing relevant future scenarios [322], for example, hospital bed needs could be overprojected for Greece by upto 25% if the severity-mix concept were not applied. The estimates presented demonstrate a fifty-fifty contribution of hospital inpatient days for chronic and late stages, despite the relatively short duration of the latter (just over one quarter of the former). Furthermore, as it can be assumed that the intensity-of-care in terms of nursing, specialist consultations and drugs is higher for an LS-inpatient day than for a CS-inpatient day, the implication for AIDS hospital costs is that the majority of these will be spend on late-stage PWAs. Furthermore, we have observed that our rankings of country-specific hospital resource needs are generally in line with epidemiologic impact, however in Italy and Greece rankings change due to relatively high outpatient involvement in AIDS hospital care.

We conclude that international comparison of AIDS care is possible using standardized methods for health-care data gathering and epidemiological modelling. Illustrated by a comparison of Dutch and Greek figures, we showed that differences can be explained considering characteristics of the health care systems. It is yet not possible to draw strict policy conclusions from our comparison of Greek and Dutch AIDS care, for example in the sense that it might be useful for Dutch authorities to consider the option of more outpatient care, or for Greek authorities to consider easing the access to inpatient care. Further research is needed and health effects of AIDS hospital care should be considered as well. Explanation of any differences between survival times between Greek and Dutch patients would then certainly need a more detailed standardization for the diagnostic case mix than applied here. Therefore, future research would certainly require to continue and compare the national databases used, extend the number and level-of-detail of analyses and validate their representativeness for the national situation.

Chapter 10

General Discussion and Main Conclusions

This chapter is partly based on book contributions:

JC Jager, MJ Postma, K Tolley, J Kennelly: **Assessment of the Socio-economic Impact of AIDS; from national towards multinational scenarios.** *In:* D Fitzsimons, V Hardy, K Tolley (Eds) *The Economic and Social Impact of AIDS in Europe*. London: Cassell 1995, pp 40-53.

MJ Postma, H Kornarou, V Paparizos, R Leidl, K Tolley, J Kyriopoulos, JC Jager for the European Research Team on AIDS Scenarios: **Hospital Care for Persons with AIDS in Greece and the Netherlands; assessment of current and future impact.** *In:* J Kyriopoulos (Ed) *AIDS Cost Analysis and Patient Classification* (in press).

10.1 The Objectives Revisited

This thesis addresses the economic impact of HIV/AIDS in the Netherlands and the European Union (EU) as a whole. It provides descriptions of methods to link epidemiological modelling to economic information for scenario analysis on AIDS impacts. The chapters refer to different methodological and empirical estimation issues. First, methods to estimate parameter values for models of AIDS economic impact are treated (chapters 3 and 4) as indicated in one of the objectives of this thesis. Second, methodological aspects of linking population-dynamical and statistical epidemiological models and economic information are dealt with in chapters 4, 5 and 7, with explicit consideration given to resource utilization and costs in different stages of the disease. Also, chapter 7 addresses quality criteria for economic impact studies attributing to the development of the Standardised Costing Framework for HIV/AIDS hospital care. For planning purposes, potential future trends in the epidemic have been translated into health-care resource needs and corresponding costs at the national (chapters 5 and 9) and EU-level (chapters 4, 8 and 9). Chapter 6 deals with a requested application of the AIDS-impact model for policy-making, estimating the impact of AIDS on life insurance. The comparability of AIDS impacts on hospital resource utilization in different countries and with other diseases is treated in chapter 9 and the Annex of this thesis. Some issues surpassing the level of an individual chapter are stressed in the current concluding chapter. These issues relate for example to checking resource-need projections for years that have yet gone by, broadening the hospital costing viewpoint to other health-care sectors, policy implications of the scenario work (at the national and EU-levels) and methodological aspects of linking epidemiological models and economic information (incidence-based versus prevalence-based impact calculus). This final chapter concludes with evaluating all the objectives in the same order as presented in chapter 1.

10.2 Disease-staging and Cost-standardization of HIV/AIDS

Previously, doubts have been expressed about the quality of published estimates of the costs of HIV/AIDS hospital treatment and care produced for EU-countries [66,218]. The explicit use of a standardised framework for cost estimation would help improve the quality of methods in studies on resource utilization and costs and enhance the comparability of cost estimates produced. This maximises their usefulness for a range of research

and policy purposes at the local, national and multi-national levels. Within the Standardised Hospital Costing Framework (SHCF) features of good quality studies are defined and these have been applied to EU-studies on hospital costs. Features of good quality refer to representativeness, the possibility of disaggregation, producing homogeneous cost groups and adherence to elementary standards of cost-of-illness studies. The SHCF is not intended to be a prescriptive instrument. It is used retrospectively for reviewing existing cost studies and can be prospectively used for helping in the development and conduction of new cost studies. The framework represents a combination of good costing practice and technical standards for cost estimation. An important area with uncertainty about the best method to employ is the choice of the patient classification system for HIV/AIDS stages (for example, CDC-stages, CD4-cell counts, viral load, AIDS-defining diagnoses or stages derived from variation in health-care resource utilization) [346]. Whatever classification is used, if it is to be useful for prospective financing and projection of health care it should reflect severity of illness, as this has been found to be the major indicator of variation in health-care resource utilization [347].

Profiles on hospital inpatient days utilization during the AIDS-stage show that a major part of health-care resources are utilized in the terminal phase. This is an important finding with respect to the previous section in that hospital resource utilization and cost studies ought to be standardized according to the patient distribution over terminal and non-terminal phases. The empirical approach chosen differentiates two substages: the final half year of AIDS preceding death (*late* stage) and the foregoing period (*chronic* stage). As illustrated in this thesis, hospital inpatient days utilization and hospital costs in the late stage are several times those in the chronic stage. Next to the need for standardizing the patient population, chapter 7 convincingly shows the importance of disease-staging for providing valid future projections under a range of assumptions. In particular in the situation of HIV/AIDS with rapid medical developments and related improvements in survival, neglect of disease-staging is shown to overproject hospital bed needs and costs by almost 15% over a period of five years into the future. Of course, further improvements in projection might be attained by distinguishing more than two substages.

Obviously, this staging concept is also relevant for other diseases. As studies from the US showed, ppy health-care costs and hospital discharges in the last year of life amount to approximately seven times those in other stages of disease. Gathering comparable information and developing similar methodology on diseases such as respiratory disease, cardiovascular disease and cancer, is needed and could benefit policy decisions in these fields. For example, Koopmanschap *et al.* illustrated the importance of choosing an

appropriate disease-staging for constructing future scenarios on Dutch cancer costs [348]. They introduce three stages: an incidence phase, an intermediate phase and a last year. Their analysis shows that - under specific assumptions - a prevalence-based model neglecting disease-stages might overproject cancer costs in 2005 by up to 20%. Although the disease-stagings for cancer and HIV/AIDS are still rather crude in only accounting for the major dynamics in disease progression, the type of conclusions reached are rather similar: neglecting disease-staging might significantly misproject health-care resources and costs in future scenarios. Staging of disease for economic reasons can follow different strategies, depending on purpose, disease characteristic and data availability; they typically have to be developed, motivated and tested just as any other analytical concept in economic evaluation and costing.

10.3 Linking Epidemiology and Economics

Results of epidemiological models and economic information can be linked prevalence-based or incidence-based to assess and project health-care resources and costs. Traditionally, health economic research uses two basic methods for expressing the economic impact of disease, labelled incidence-based and prevalence-based methods [40]. The first concerns accounting lifetime health-care resources to the year of incidence of disease (*see* chapters 7 and 9). The second method concerns an annualization of these lifetime health-care resources (*see* for example, chapters 5 and 8). To cover the full economic impact of a health-care intervention, it is necessary to analyse the lifetime consequences for resource needs incurred by a representative case. This incidence-based approach does however assume that the future health-care technologies will remain the same as in the analysis, and also extends all other assumptions up to the time until the last incident case has been dealt with. If the assumption of everything staying equal holds true for the period of analysis, and if the full economic impact is what is being referred to in a decision context (for example, in decisions on prevention investments/budgets), the incidence-based approach is the more appropriate one. If on the other hand, the budget impact of a health-care technology is the focus of analysis, and if this impact is expected to change with new treatment technologies, then the prevalence-based approach, applied over a well-defined period of analysis, will be more appropriate to support decisions on the economic side. With respect to the full economic impact both methods are myopic. On the short-term however, the incidence and prevalence-based approaches may differ

even when applied to the same epidemiologic data set. As an example, the recent introduction of Highly Active Antiretroviral Therapy (HAART) in HIV treatment may serve. On the short-term HAART seems to cause major improvements in health and related cuts in hospitalizations. As a consequence, prevalence-based assessment for budgeting purposes one or two years ahead indicates reductions in hospital budgets for HIV/AIDS care [349]. However, resource-intensive and costly late stages of HIV/AIDS are merely shifted a few years ahead and on a lifetime basis costs will rise, also because HAART is quite expensive. An incidence-based approach would typically show the latter development, whereas a prevalence-based approach might focus on the short-term cost reductions only. In consequence, implications drawn for health policy might differ depending on the approach and presentation used. Obviously, the framework for linking epidemiology and economics should encompass the possibility of using both types of assessments and projections. The developed framework in this thesis satisfies this condition. Finally and completing the developed framework, confidence intervals and sensitivity analyses have been elaborated for various aspects (for example, per person-year monetary costs of AIDS and the duration of stay in the AIDS-stage).

10.4 Dutch Scenario Results

At the time we performed the Dutch AIDS scenario study (chapter 4) reliable national data on hospital resource utilization for the new disease HIV/AIDS were lacking [350]. During the 1990s the coding of HIV/AIDS hospital care has become integrated in the routine daily hospital administration [351]. Over 99% of Dutch hospitals contribute to the national hospital register of SIG Health Care Information (Utrecht). In 1993, hospital inpatient days for HIV/AIDS as *primary* diagnosis amounted to 20 600 for AIDS and 2300 for the pre-AIDS stages (codes 042 for AIDS, 043 for AIDS Related Complex and 044 for other HIV). The estimate for hospital inpatient days in 1993 amounts to 39 900 for AIDS and 5400 for the pre-AIDS stages (chapter 5). Using more recent information that possibly better reflects hospital practice in the 1990s, the figure for AIDS was updated to 30 100 in chapter 9. An important drawback for comparing the estimation and the registration involves the classification systems used, that do not entirely match. The estimates are based on the AIDS surveillance case definition, whereas the national registration applies the 9th revision of the International Classification of Diseases. Because the AIDS surveillance case definition includes slightly more disease complicati-

ons than code 042 of the Classification of Diseases does, there is probably a better match if an unknown part of the inpatient days in the national register with AIDS as additional diagnosis were included. The national figures for HIV/AIDS as any (primary or additional) diagnosis were 60 000, including 54 200 days for AIDS. The combined estimate of chapters 5 and 9 of 35 600 inpatient days is now inbetween the nationally registered figures for HIV/AIDS as primary and as any diagnosis. This suggests that the estimates are in line with the national hospital registration. In consequence, the extrapolation of results of individual Dutch hospital studies seems to provide valid results for the national level. Furthermore, this extrapolation methodology has a major advantage when applied to other countries and the EU as a whole (chapters 8 and 9). Many other European countries lack an accessible national hospital register and hospital impact must necessarily be based on individual hospital studies.

In order to provide an indication of the monetary costs that are involved with the figures on hospital care one can elaborate on Dutch estimates of the costs of a hospital inpatient day, a hospital outpatient hospital visit and a day-care hospital contact that are available for 1990 [35]. Since then these costs per contact have increased due to price increases of inputs in hospital care - for example, salaries and investments in new technologies - and to increases in the care-intensity of a hospital contact - for example, the number of procedures during an inpatient day or outpatient contact [352]. Corrected for price increases due to both factors the respective cost figures in 1995 ECUs are 328 (inpatient day) and 125 (outpatient contact; including day care)³⁴. Multiplication with the respective number of days and contacts results in 13.9 million ECUs, corresponding to 0.18% of the 1995 national budget for hospital care. This figure roughly corresponds to what was projected in chapter 5 for AIDS-related inpatient and outpatient hospital care in 1995 in one of three scenarios presented.

Combining the statistical methodology elaborated in chapter 9 and the monetary cost estimates of table 5.2 enables the estimation of lifetime hospital costs. In chapter 7 this type of calculation was used to motivate the application of a staged instead of a non-staged model, here we estimate the lifetime costs *persé*. In the reference scenario, as defined in chapters 8 and 9 for the Netherlands, lifetime hospital costs amount to 43 850 ECUs (95%-confidence interval for an individual PWA: 2260 - 107 700 ECUs). This figure underestimates the total lifetime hospital costs per person for groups of HIV-

³⁴ To transform the 1990 cost level to the 1995 level a nominal growth factor of 1.24 and a factor for intensity-of-care increases of 1.10 is used [352]. For the exchange of Dutch guilders (f) into ECUs an exchange rate of 1 ECU equals f2.12 is used.

infected persons who survive longer than 2 years in the AIDS stage. Lifetime pre-AIDS hospital costs can be derived straightforward from chapter 5 to amount 23 100 ECUs. In an overview on the economic impact of AIDS in Europe, Jager *et al.* [107] provided an extension of the Dutch scenarios on hospital impacts to other sectors of health care. For patients in the pre-AIDS stages they estimated costs per person-year (ppy) of 120 ECUs for the GP and 4 120 ECUs for early AZT-treatment (500 mg/day), during respectively 7 and 1 years in average. For PWAs these ppy costs amount to 280 ECUs for the GP, 605 ECUs for home care (district nurse), 615 ECUs for home help and 375 ECUs for the nursing home. Elaborating on the expected lifetime hospital costs, total lifetime health-care costs would be 75 700 ECUs. So, on total lifetime health-care costs the share of non-hospital costs is estimated to be relatively small with only 12%. In future projections of the total health-care costs it was however shown that the share of home care grows in all scenarios investigated. This is a consequence of epidemiological developments solely, and the Dutch government policy of substituting home care for hospital care might be expected to sharpen this trend. In order to adequately monitor developments in the costs of HIV/AIDS it is necessary to set up a patient-based monitoring system in home care that is analogous to the one already existing in the hospital sector.

10.5 Extension of EU-results on Hospital Care

For the EU-level this thesis focusses on the impact of the AIDS-stage on the hospital resource needs (chapter 8) and hospital costs (chapter 4). Tolley *et al.* [276] provide some details from a review of EU cost studies published between 1985-1995. It was possible to make comparisons of inpatient and outpatient costs and to a limited extent of day-care costs, by AIDS and pre-AIDS stages for a number of EU-countries [95,353,354]. This review enables the update of the EU cost figures in chapter 4 to reflect the 1999 monetary cost projection. For this purpose, costs have been transformed from original price year and local currency to 1993 ECUs, using country-specific health-care expenditure price indices and the latest available health-care-specific purchasing power parities [355]. Resulting hospital costs ppy in the period 1988-1992 are between 20-40 thousand ECUs for AIDS patients across a range of EU-countries. In combination with the various scenarios this range indicates total hospital costs in 1999 to vary between 1.1 and 3.4 billion ECUs, compared to the baseline level around 0.8 - 1.6 billion ECUs in 1993. If the upper limit were the actual figure, 1999 hospital costs would reflect over 1% of the

current health-care expenditure of all EU-countries. One should realize though that these future projections don't include any trends in ppy hospital costs.

Whereas utilization has declined over time in the late eighties and early nineties in all studies and countries for which trend data are available, any changes in hospital costs ppy have been far less dramatic [62,65,153,285,286-288]. Possible explanations are that the intensity of care and unit costs of resources have increased and more expensive medications have been introduced. For example, the recent introduction of antiretroviral combination triple therapy involves relatively high costs of approximately 15 000 ECUs per year [356]. However, as a consequence of the new therapy, cuts in HIV/AIDS hospitalizations have been reported in Los Angeles, New York and France [357-359]. Another study shows that benefits of averted hospital care might even surpass the incremental costs associated to the new therapy [360]. The calculations in chapter 8 on hospital bed needs for the EU after widespread introduction of triple combination therapy indeed show that significant reductions in prevalence-based calculated bed needs might result. As mentioned, it can be assumed that the costly (late) AIDS-stage is merely postponed and not prevented, and lifetime hospital bed needs and costs per HIV-infected person increase.

Tolley *et al.* [276] indicate that hospital costs are between 2 thousand (asymptomatic HIV in the UK in the period 1987-1989) and 10 thousand (symptomatic HIV in Spain in 1990) ECUs ppy for pre-AIDS stage patients, corresponding to 5 % and 40 % of the corresponding AIDS figures. In particular, levels of ppy inpatient days are significantly lower for the pre-AIDS stages, whereas the outpatient hospital utilization levels for AIDS and pre-AIDS stages are quite similar. For example, in one French study outpatient visits equal in both stages at approximately seven ppy [281]. Jager *et al.* [107] extended the preliminary scenario results of chapter 4 to encompass some of the indirect costs as well. In particular, they focus on the potential years of life lost (PYLL) due AIDS deaths. PYLL provide a proxy of indirect costs of HIV/AIDS in the EU, as a monetary value of the life years lost has not been estimated. Using an annual incidence-based procedure, they estimated the number of PYLL at the end of the century to range between 203 800 and 520 500. As illustrated by a number of studies [144,361,362] and for some selected EU-countries, PYLL for AIDS has surpassed those due to other infectious diseases and is in the order of magnitude of those due to suicide and road accidents. Recently, a possible doubling of PYLL up to the year 2000 in the Netherlands compared to the 1990-level has been indicated by Jager *et al.* [111]. It is shown that PYLL due to AIDS approaches those of diabetes, several types of cancer and chronic respiratory disease.

10.6 Impact of Scenario Analysis on Health-care Policies

The scenario analysis for HIV/AIDS in the Netherlands influenced the development of health-care policies at the national and the international level. At the national level, the summary and recommendations of the Scenario Study [101] were passed through to the delegates of the Dutch Lower House to serve in the discussions on AIDS-policies in 1992 [363]. A specific request referred to an advise on the global cost-effectiveness of the national budget of 944 000 ECUs for campaigns and projects to prevent the further spread of HIV within the Dutch population [364]. Discounting the lifetime hospital costs per HIV-infected person at 5% per year for 14 years between infection and death, it may be argued, from an economic point of view, that such budget would start to be cost-effective if more than approximately 20 new infections would be prevented on an annual basis. This seems quite feasible. Moreover, if the indirect costs of HIV infection were taken into account, one could qualify the budget as cost-effective with even fewer new infections prevented required. Thus there was an economic argument in favour of the present prevention budget unless of course the budget could be spent on another disease prevention area that has a better cost-effectiveness ratio.

In chapter 6 the request for a study on the impact of AIDS on life insurance was discussed. Also, some economic analyses in HIV prevention and treatment drew on work performed in the Scenario Study. For example, cost-effectiveness of HIV combination-therapy after percutaneous exposures of Dutch medical personell was calculated at £20 300 - 88 600 net direct costs per life-year gained [365]. The study suggests a sharpening of indication to improve cost-effectiveness. Furthermore, in 1990 a study on the evaluation of HIV screening among pregnant women in Amsterdam was started. One of the goals of the study was to investigate the cost-benefit ratio [366]. Benefits were thought to occur through possibly preventing the birth of an HIV-infected child and associated health-care costs, if an HIV-infected pregnant woman decides to terminate pregnancy. Costing figures derived from the Scenario Study were used. At present, an evaluation study of HIV-screening is much more complex since several new factors have proven to affect both the vertical transmission probability and the costs, such as AZT/Zidovudine treatment during and after pregnancy, breast-feeding versus formula feeding and an elective ceasarian section. Furthermore, early detection of HIV-infection through screening and early uptake of antiretroviral treatment might also have beneficial effects on the progression of HIV in the mother. To cover these recent developments and insights a model has been developed and a first application to England has been elabora-

ted [367-370].

From the start of the Dutch Scenario Study, it was the objective to build a scenario analytic approach that could easily be extended to foreign situations [100]. Therefore, the methodology of the approach and the illustrative results for the Netherlands have often been highlighted at international conferences. Furthermore, the Dutch Scenario Team was involved in meetings of several working groups of the EU and the World Health Organization on the economic impact of AIDS [109,110,303,304,371]. National study groups from Greece, Spain and France were advised on scenario construction for their respective countries [274,372-374]. In addition, future projects on the costs of AIDS in France and Belgium were drawn up with explicit reference to our scenario methodology [374,375]. During 1993 the finalized Dutch Scenario Study and related publications were crucial for being assigned with the grant for multi-national AIDS scenarios (EU-grant PL941723 of DG XII). A preliminary version of chapter 8 of this thesis was integrated in the final report of another EU-project in DG V [95]. As illustrated in Chapter 9 of this thesis, the standardized scenario analytic approach enables international comparisons. So in consequence, a monitoring system of AIDS impacts in Europe has been developed that addresses the wide range of epidemiology, economic aspects and societal responses. The importance of such a system was stressed by the Council of Europe in 1992, in order to enable a proper timing of rapid reaction procedures to new emerging developments in the HIV/AIDS epidemic, treatments and care [376]. More recently, a similar argument was published *Vaccine* [377]. Finally, during the international AIDS Conference in Vancouver the need for standardized procedures on performing economic impact assessments to help health-care policy development was stressed [378].

The studies on AIDS scenario analysis in this thesis, provide an example of scenario analysis in infectious diseases. As infectious diseases exhibit their characteristic dynamics, extension of the "traditional" cost-of-illness approach is motivated in his thesis. This extended approach is labelled dynamic cost-of-illness assessment. Combining this approach with scenario analysis - where a set of different assumptions on core-parameters is investigated - provides the basis for cost-effectiveness analysis in infectious disease prevention and treatment [379]. Above, examples on cost-effectiveness analysis of HIV-screening in pregnant women and post-exposure HIV prophylaxis were mentioned. Examples of the extension of the approach to other infectious diseases refer to screening for *Chlamydia trachomatis* [380-382] and Influenza vaccination [383-385]. Scenario analysis has already been mentioned as an integral part of cost-effectiveness [31], and this

seems to be true in particular for infectious diseases. Other specific features of cost-effectiveness analysis in infectious diseases illustrated in this thesis refer to the linkage with a model for the spread of the disease and the importance of sound costing figures on lifetime and per person-year basis. Ultimately, this thesis seeks to attribute to the development of guidelines for cost-effectiveness in infectious diseases [386,387].

10.7 Main Conclusions

Guidelines should be applied for the estimation of HIV/AIDS-related personal health-care costs, allowing valid comparisons between studies performed at different times and settings by different researchers. (objective 1; chapters 3 and 7)

In general, there is a need for a standardized approach to cost-of-illness studies to increase the comparability of studies. (objective 2; chapters 4 and 7)

The choice of an appropriate disease-staging averts structural biases in projections of hospital care and costs. (objective 3; chapters 5,7 and 8)

Estimates of the resources and costs of hospital care for HIV/AIDS can be used for planning at the national or multi-national level if a standardized/generic approach in epidemiological modelling, data-gathering and severity-staging is applied. (objective 4; chapters 3 and 4)

In the Netherlands, ppy hospital costs in the late stage of CDC IV are almost threefold those in the chronic CDC-IV stage. Lifetime costs from the time of HIV-infection onwards are estimated to amount 76 000 ECUs, hospital costs constitute almost 90% of this figure. (objective 5; chapters 5 and 9)

Studies in several EU-countries show that utilization of hospital inpatient days in the care-intensive late stage of AIDS is twice to tenfold that in the chronic stage. In most investigated countries total hospital contacts in the chronic stage are approximately half of those in the late stage. (objective 5; chapter 8)

Dutch scenarios demonstrate that approximately one quarter to a half percent of total

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hospital costs will be required for HIV/AIDS by the end of the century, a sizeable but probably manageable proportion. Cost projections in several scenarios indicate a range for AIDS hospital costs of 0.5 and 1.0% of total EU-expenditures on hospital care by the end of the century. (objective 6; chapters 3, 5 and 10).

Hospital bed needs for AIDS in the EU will amount to 0.5% to 0.65% of all hospital beds available in the EU. Sensitivity analysis shows that new combination triple therapy might lower the estimate for hospital beds by 20-30%. (objective 6; chapter 8)

Statistical confidence limits in combination with several scenarios on hospital bed needs for AIDS by the end of the century, indicate a range of 0.2% to 0.3% of currently available hospital beds in the Netherlands. (objective 6; chapters 5 and 9)

Projected hospital bed needs in the Netherlands for HIV/AIDS by the end of the century are limited compared to projections for coronary heart disease, stroke and diabetes. (objective 7; chapter 5 and annex)

Quantitative information on hospital care for AIDS indicates that it is organised differently in the various EU-countries, varying from high inpatient (France) or outpatient (Greece) involvements to a mixed organisation form (Netherlands). (objective 7; chapter 8)

Differences in AIDS care between two selected countries can be explained from differences in the respective health-care systems. (objective 8; chapter 9)

Scenario analysis on economic impacts of HIV/AIDS has influenced the development of health-care policies at the national - advise on life-insurance impact, planning and economic evaluation - and international level - advisory role in set-up of foreign AIDS scenario studies. (objective 9; chapter 6,9 and 10)

The dynamic cost-of-illness approach for HIV/AIDS can be applied to other infectious diseases and therefore merely serves as an illustration for analyses in, for example Influenza and *Chlamydia trachomatis*. (objective 10; chapter 10)

The scenario analytic approach can be integrated in HIV/AIDS cost-effectiveness analysis

(objective 11; chapter 10)

In this thesis a dynamic cost-of-illness approach has been developed for HIV/AIDS. The approach esteems the importance of linking cost-of-illness with epidemiological modelling into future scenarios. Further, the relevance of disease staging in costing and scenario analysis has been demonstrated and deserves broad attention in the standardization of costing methods. Future research should be directed to the development of dynamic cost-effectiveness analysis of treatment and prevention for infectious diseases. This type of research is currently in progress in both national and international initiatives [388,389]

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Annex

Projecting Utilization of Hospital In-patient Days in The Netherlands; a time-series analysis

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Projecting utilization of hospital in-patient days in The Netherlands: A time-series analysis

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The object was to model and project utilization of hospital in-patient days for selected diseases in The Netherlands. We used sex- and age-specific standardized monthly utilization of hospital in-patient days during 1980–90 for lung cancer, diabetes, coronary heart disease, stroke, and pneumonia. These data were supplied by the Health Care Information Centre (Stichting Informatiecentrum voor de Gezondheidszorg). We applied Box–Jenkins time-series analysis seasonal autoregressive integrated moving-average (SARIMA) models. Estimated models are tested by considering the Portmanteau test and the Akaike information criterion. SARIMA models give an adequate representation of hospital-in-patient-days utilization for the major sex and age classes of most selected diseases. Poor modelling results are obtained for diabetes in all sex and age groups and in elderly women with coronary heart disease or with stroke. Seasonality is an important factor in most of the models that we have estimated, particularly for utilization of pneumonia and stroke patients. The major trends in standardized in-patient days are downward, and projected 1995 levels of *standardized* utilization are below the 1990 levels for all the selected diseases. *Population-based projections* for 1995 are lower than the 1990 projections only for lung cancer and diabetes. The adequacy of the SARIMA models appears to be sensitive with respect to the parameter in the Portmanteau test. We discuss two possible explanatory developments for in-patient-days utilization: (i) developments in the provision of hospital care, and (ii) epidemiological developments. The selected diseases showed a decreasing mean duration of stay in 1980–90. Only for coronary heart disease did a rise in discharges in the same period outweigh this trend. We assessed contrasts between published epidemiological developments and the trends in in-patient-days utilization. Possible explanations concern shifts from in-patient to out-patient care and changes in treatment. Finally, complementary to our SARIMA models, the investigation of future in-patient days utilization by means of scenario analytic approaches remains important.

Keywords: time series; SARIMA model; hospital care; projection; health-care planning.

1. Introduction

A range of factors influence the utilization of health care. In The Netherlands, the main pressures on utilization are an ageing population, an increase in the demand for out-patient care, and advancements in medical technology. However, a decreasing average length of hospital stay and effective preventive interventions appear to be having a controlling effect on utilization. The influences of such factors are likely to differ for each disease, and analysis of their relative importance will require a disease-specific approach. The impact on health-care utilization will also depend on trends in the prevalence of disease.

The *Financial Overview on Care Provision* [1] is an annual governmental report of the financial and resource policy for health-care provision in The Netherlands. This policy is based on an extrapolation of past developments in health-care utilization and expected future developments. However, there is no explicit consideration of the impact of trends in the occurrence of diseases on utilization and policy setting. In this paper we examine the impact of developments in the occurrence of diseases on health-care utilization in The Netherlands.

Analysis of disease-specific health-care utilization has been undertaken in research coordinated by the Steering Committee on Future Health Scenarios (Stuurgroep Toekomstscenario's Gezondheidszorg: STG) [2-5]. Ideally, this type of research requires information on demographical and epidemiological developments (number of patients) and trends in the utilization of health-care for each patient. However, such data is not extensively available and it has only been used to a limited extent in the STG projects [5]. Our study uses a time-series analytical method applied to standardized resource-utilization data, reflecting a combination of epidemiological developments and patient-based trends in service utilization.

Disease-specific utilization data for the whole Dutch population is available for a number of health-service indicators. For example, in-patient hospital care, nursing-home care, and in-patient-psychiatric-care data is available from the SIG Health Care Information Centre in Utrecht (Stichting Informatiecentrum voor de Gezondheidszorg: SIG). In our study we focus on the utilization of hospital in-patient care, using in-patient days as the utilization indicator, since this is a substantial element of the total cost of health care (hospital costs were one-third of the total cost of health care in The Netherlands in 1993 [1]). Specific diseases which reflect the range of factors influencing resource utilization have been selected for analysis. These are lung cancer, diabetes, coronary heart disease, stroke, and pneumonia. Twelve per cent of hospital in-patient days were associated with these diseases in 1990. In addition, we have already incorporated these diseases in an integral model of public health. Our analysis is sex and age specific to allow for ageing effects on the utilization of hospital in-patient-days [6]. This approach goes beyond the use of traditional resource-utilization scenario techniques, which use cross-sectional data on resource utilization for different diseases [7], or use data on trends but do not distinguish by disease [8]. We know of only one previous application of time-series analysis to resource-utilization data; this was for specific chronic conditions associated with alcohol abuse [9].

The results can contribute to the rational planning of hospital beds over time for

different diseases and across hospital specialities. In the next stage of research we plan to develop and further apply the methodology for examining disease-specific patterns in order to inform the Ministry of Health, Welfare and Sports on planning future resources for health care [10].

2. Data and methods

2.1 Data and basic data management

We use data available from the SIG on the monthly utilization of hospital in-patient days for the period 1980–90. Data on utilization of hospital facilities is sent to the SIG by all academic, general, and specialist hospitals in The Netherlands. The use of monthly data allows the application of accurate methods of modelling and projection.

The SIG attributes all the days of an in-patient stay to the month of admission. For an economic analysis this is insufficient because it does not reflect the actual monthly utilization of scarce health-care resources. Therefore, using a computer program developed in cooperation with the SIG, we have adjusted the data to record the actual number of in-patients days for the month in which they occur. If an in-patient stay exceeds one calendar month, the total number of days are divided over the respective months.

Disaggregated analysis is undertaken using the six age categories: 0–14, 15–24, 25–44, 45–64, 65–74, and 75+ (some of the analysis was conducted at a more detailed level). International classification of diseases (ICD) codes for the primary diagnosis are used to define the disease corresponding to the in-patient days [11]. The ICD code at discharge is used since this is more reliable than the code at admission. The respective ICD codes for lung cancer, diabetes, coronary heart disease, stroke, and pneumonia are 162, 250, 410–414, 430–438, and 480–486. The quality of the process of ICD coding in the individual hospital is safeguarded adequately. Explicit attention is given to the accuracy of the computerized recording of data by the hospital's medical registrar, and cross-checks exist to verify the reliability of the data. However, we do not know of any research that has evaluated the quality of the ICD coding process.

Sex- and age-specific utilization data is *standardized* with reference to the mean Dutch population of 1990, using the midpoint population halfway each month during 1980–90. The mean population of 1990 is defined as the sum of the population sizes on 1 January and 31 December divided by two. A linear change in the population over one year is assumed in the calculation of midpoint population figures for the period 1980–90. Population data is supplied by the Central Bureau of Statistics in Rijswijk (Centraal Bureau voor de Statistiek: CBS).

By 1990 all hospitals in The Netherlands supplied their data to the SIG. Previously this was not the case. For example, 2.5% of the hospitals did not supply data in 1986, and some specialist hospitals (eye clinics and cancer centres) only started supplying data to the SIG very recently. To ensure consistent and nonbiased time series we raise in-patient days for years with only partial participation by means of *simulated* disease-, sex-, and age-specific discharges. The simulations are consistent with the size and structure of the missing hospitals and they take into account the demographic

characteristics of the population served by these hospitals. Finally, we assume that the registered average length of stay applies to simulated discharges for calculating simulated in-patient days. Because of missing data, discharges can only be simulated for the year 1984 onwards—for 1980–83 we assume the same disease-, sex-, and age-specific associations between observed and simulated in-patient days as were calculated for 1984. This basic data management produces 12 time-series of standardized hospital-in-patient-days utilization (i.e. 2 sex and 6 age categories) for each disease, with 132 monthly observations per series (covering 11 years).

2.2 Analytical framework

We use the Box–Jenkins statistical technique [12] to analyse the time series, specifying seasonal autoregressive integrated moving-average (SARIMA) models. (For two time series the number of nonzero observations is insufficient for analysis and we use the overall mean as a model.) For this purpose a time series $\{X_t\}$ ($t = 1, \dots, 132$) is conceived to represent a series of observations within a system that is influenced by several factors. The approach is suited to model dependencies between successive observations (trend and seasonal pattern) by making a distinction between structural relationships and chance occurrences. It describes the behaviour of the system without the need for exploratory data on factors such as developments in epidemiology and in the provision of hospital care. These developments are *implicitly* incorporated in the resulting model. The form of the SARIMA model is specified by seven parameters p, d, q, P, D, Q, s with the notation $\text{SARIMA}(p, d, q) \times (P, D, Q)_s$ [12]. The parameter s indicates the seasonal lag s (here s equals 12 months), with the parameters P, D , and Q defining the seasonal model structure. The other parameters refer to the overall model. In mathematical terms the general form is

$$\phi(B)\Phi(B^{12})(1-B)^d(1-B^{12})^D X_t = \theta(B)\Theta(B^{12})\varepsilon_t \quad (t = 1, \dots, 132), \quad (2.1)$$

with

$$\begin{aligned} B^k(X_t) &= B^{k-1}B(X_{t-1}) = \dots = X_{t-k}, \\ \phi(B) &= (1 - \phi_1 B - \phi_2 B^2 - \dots - \phi_p B^p), \\ \Phi(B) &= (1 - \Phi_1 B^{12} - \Phi_2 B^{24} - \dots - \Phi_P B^{12P}), \\ \theta(B) &= (1 - \theta_1 B - \theta_2 B^2 - \dots - \theta_q B^q), \\ \Theta(B) &= (1 - \Theta_1 B^{12} - \Theta_2 B^{24} - \dots - \Theta_Q B^{12Q}), \end{aligned}$$

assuming all chance epsilons to be identically and independently normally distributed with a zero mean and a constant variance. Therefore p and P indicate the orders of the autoregressive parts of the model, and q and Q are those of the moving-average parts. In practice a nonzero d can be interpreted as indicating a trend in the mean level of the series, whereas a nonzero D might indicate the presence of a significant seasonal effect. To remain within acceptable confidence limits of the projections, we extrapolate standardized utilization of hospital in-patient days only for the period 1991–95 $\{X_t\}$ ($t = 133, \dots, 192$).

A time series is nonstationary if the standard deviation of the observation depends systematically on the mean of the observations (heteroscedasticity). We transform a heteroscedastic time series $\{X_t\}$ into a homoscedastic one $\{Y_t\}$ by

$$Y_t = \ln(X_t) \quad (t = 1, \dots, 132), \quad (2.2)$$

and we replace Y_t for X_t in expression (2.1).

To test for nonstationarity we cut the series into 11 equal (yearly) parts of 12 observations. For each part we calculate the mean and the standard deviation. The logarithmic transformation is applied if regression of the standard deviation on the mean exhibits a significant linear relation (two-sided t -test; $p < 0.05$). In case the projected untransformed utilization of in-patient days becomes negative in the short term, we also apply the logarithmic transformation.

Finally, the projected logarithmic utilization of in-patient days is transformed back into real projections (X'_t) using

$$X'_t = \exp(Y_t) \quad (t = 133, \dots, 192), \quad (2.3)$$

with X_t and X'_t ($t = 133, \dots, 192$) providing *median-unbiased estimators* of the median future-in-patient-days utilization [13–15]. An estimator is median unbiased if the median of its distribution equals the parameter to be estimated. There are both theoretical and practical reasons for choosing the median as the measure of the central tendency [16].

The orders p, d, q, P, D, Q in the SARIMA model are identified by studying the *autocorrelation function* and the *partial autocorrelation function* [12]. Next, a maximum-likelihood procedure is used to estimate the parameter values in the model. Specification of the SARIMA model is conducted using an interactive computer program designed in S-PLUS [17, 18].

To test the model we use graphical inspection of the residual autocorrelations, the Portmanteau test and the Akaike information criterion. The graphical pattern of the residual autocorrelations should not include too many values outside the range $[-2/N^{-1/2}, +2/N^{-1/2}]$. As these autocorrelations differ significantly from zero ($p < 0.05$) the wrong choice of model is indicated [12]. If none, one, or two residual autocorrelations differ significantly from zero with no obvious interpretation in reality there would be insufficient evidence to reject the model [19, 20]. The Portmanteau test statistic involves the first M residual autocorrelations as a whole [21]. The test statistic is approximately chi-squared distributed with $(M - p - q - P - Q)$ degrees of freedom. The approximation is acceptable if the number of observations exceeds 100 [22]. We report the p -values of the Portmanteau test statistic with M equalling 36.

We compare different models for the same time series using the Akaike information criterion [23]. This criterion involves the likelihood of the model penalized for the number of independent parameters. Therefore, an increase in likelihood can be accompanied with a decrease of the Akaike information criterion if the number of parameters is increased.

Furthermore we apply the population forecasts of the CBS to transform *standardized* future utilization into *population-based utilization*. This enables the population-based projections to include the effects of the ageing in the Dutch population.

3. Results

The orders of each estimated SARIMA model and the corresponding p -value for the Portmanteau test are presented in Table 1. The adequacy of the estimated models varies. In general, the models for lung cancer and diabetes do not perform well, although estimated models for men aged 65–74 have acceptably low p -values. Men aged 65–74 form the most important age group for lung cancer. We estimate adequate models for men with coronary heart disease, especially in the two major age groups, 45–64 and 65–74. However, weak models are produced for coronary heart disease and for stroke for the most important age group for women, those aged 75+. For pneumonia the overwhelming importance of seasonal patterns enables satisfactory representation by SARIMA modelling.

TABLE 1

Estimated SARIMA model for hospital-in-patient-days utilization, the corresponding p -value for the Portmanteau test (see text), and standardized observations of annual-in-patient-days utilization (1990; in thousands) and projections (1995; in thousands)

Disease	Sex	Age class	Model characteristics		In-patient-days utilization	
			Order	p-value	1990	1995
Lung cancer	Male	0-14	^a		0.0	0.0
		15-24	$(1, 0, 0) \times (0, 0, 0)_{12}$	0.40	0.0	0.0
		25-44	$(0, 1, 2) \times (0, 0, 0)_{12}$	0.55	3.7	3.6
		45-64	$(0, 1, 2) \times (2, 0, 0)_{12}$	0.40	56.6	43.1
		65-74	$(0, 1, 2) \times (0, 1, 1)_{12}$	0.00	72.6	57.5
		75+	$(1, 0, 0) \times (0, 1, 1)_{12}$	0.40	41.4	45.7
	Female	0-14	$(1, 0, 0) \times (0, 0, 0)_{12}$	0.10	0.0	0.0
		15-24	$(1, 0, 0) \times (1, 0, 0)_{12}$	0.10	0.0	0.0
		25-44	$(2, 0, 0) \times (0, 0, 0)_{12}$	0.35	2.5	2.8
		45-64	$(1, 0, 0) \times (1, 0, 0)_{12}$	0.45	12.6	12.6
		65-74	$(1, 0, 0) \times (1, 0, 0)_{12}$	0.25	12.5	11.2
		75+	$(1, 0, 0) \times (1, 0, 0)_{12}$	0.50	6.4	7.1
Total				208.3	183.6	
Diabetes	Male	0-14	$(1, 0, 0) \times (1, 0, 0)_{12}$	0.25	4.3	5.1
		15-24	$(2, 0, 0) \times (1, 0, 0)_{12}$	0.25	4.3	5.0
		25-44	$(0, 1, 1) \times (0, 0, 3)_{12}$	0.60	13.5	10.4
		45-64	$(0, 1, 1) \times (1, 0, 0)_{12}$	0.50	28.7	19.9
		65-74	$(2, 0, 0) \times (3, 0, 0)_{12}$	0.05	25.0	22.7
		75+	$(2, 0, 0) \times (2, 0, 0)_{12}$	0.60	27.6	27.2
	Female	0-14	$(0, 0, 1) \times (0, 1, 1)_{12}$	0.30	4.3	4.3
		15-24	$(1, 0, 0) \times (2, 0, 0)_{12}$	0.90	4.3	5.0
		25-44	$(0, 1, 1) \times (0, 1, 1)_{12}$	0.55	10.1	5.3
		45-64	$(1, 0, 0) \times (3, 0, 0)_{12}$	0.15	28.8	24.1
		65-74	$(0, 1, 1) \times (2, 0, 0)_{12}$	0.60	51.0	32.4
		75+	$(1, 1, 1) \times (2, 0, 0)_{12}$	0.80	72.8	52.8
Total				274.3	214.2	

TABLE 1 (continued)

Disease	Sex	Age class	Model characteristics		In-patient-days utilization	
			Order	p-value	1990	1995
Coronary heart disease	Male	0-14	^a		0.0	0.0
		15-24	(1, 0, 0) × (1, 0, 0) ₁₂	0.20	0.0	0.1
		25-44	(0, 1, 1) × (0, 1, 1) ₁₂	0.20	32.2	26.3
		45-64	(0, 1, 1) × (0, 1, 1) ₁₂	0.05	253.5	231.3
		65-74	(0, 1, 1) × (0, 1, 1) ₁₂	0.05	161.6	160.4
		75+	(2, 0, 0) × (1, 0, 0) ₁₂	0.20	80.2	80.0
	Female	0-14	(1, 0, 0) × (2, 0, 0) ₁₂	0.15	0.0	0.0
		15-24	(1, 0, 0) × (0, 0, 0) ₁₂	0.75	0.0	0.0
		25-44	(2, 0, 0) × (0, 0, 0) ₁₂	0.20	5.7	6.3
		45-64	(1, 1, 1) × (0, 1, 2) ₁₂	0.65	53.6	49.4
		65-74	(2, 0, 0) × (2, 0, 0) ₁₂	0.25	100.7	100.6
		75+	(1, 0, 0) × (2, 0, 0) ₁₂	0.45	100.7	102.4
	Total				788.5	756.7
Stroke	Male	0-14	(1, 0, 0) × (0, 0, 0) ₁₂	0.05	0.7	0.7
		15-24	(1, 0, 0) × (1, 0, 0) ₁₂	0.20	1.0	1.3
		25-44	(0, 0, 2) × (3, 0, 0) ₁₂	0.25	9.4	8.0
		45-64	(0, 1, 1) × (2, 1, 0) ₁₂	0.10	69.4	60.2
		65-74	(1, 0, 0) × (0, 1, 1) ₁₂	0.20	92.4	95.3
		75+	(1, 0, 0) × (0, 1, 1) ₁₂	0.30	110.6	114.2
	Female	0-14	(1, 0, 0) × (0, 0, 0) ₁₂	0.45	0.5	0.5
		15-24	(3, 0, 0) × (0, 0, 0) ₁₂	0.35	1.3	1.4
		25-44	(1, 0, 0) × (1, 0, 0) ₁₂	0.05	11.4	11.7
		45-64	(0, 1, 1) × (0, 0, 3) ₁₂	0.55	35.0	34.4
		65-74	(1, 0, 1) × (3, 0, 0) ₁₂	0.35	87.5	83.3
		75+	(1, 0, 1) × (0, 1, 1) ₁₂	0.45	221.9	221.4
	Total				641.2	632.4
Pneumonia	Male	0-14	(2, 0, 0) × (3, 0, 0) ₁₂	0.10	20.1	17.2
		15-24	(1, 0, 1) × (3, 0, 0) ₁₂	0.50	1.9	1.1
		25-44	(1, 0, 0) × (1, 0, 0) ₁₂	0.25	7.1	7.8
		45-64	(2, 0, 0) × (2, 0, 0) ₁₂	0.05	17.0	16.9
		65-74	(4, 0, 0) × (2, 0, 0) ₁₂	0.10	23.2	22.5
		75+	(1, 0, 0) × (2, 0, 0) ₁₂	0.10	40.6	39.2
	Female	0-14	(3, 0, 0) × (2, 0, 0) ₁₂	0.30	14.0	12.8
		15-24	(1, 0, 0) × (3, 0, 0) ₁₂	0.05	1.3	1.6
		25-44	(3, 0, 0) × (3, 0, 0) ₁₂	0.05	5.8	6.1
		45-64	(2, 0, 0) × (2, 0, 0) ₁₂	0.05	7.1	7.4
		65-74	(2, 0, 0) × (2, 0, 0) ₁₂	0.10	12.7	12.9
		75+	(1, 0, 0) × (1, 0, 0) ₁₂	0.05	32.5	27.4
	Total				183.3	172.9

^a Insufficient data to estimate the SARIMA model.

FIG. 1. Standardized monthly utilization of hospital in-patient days: (—) observations (1980–1990), and (···) projections (1991–1995). (a) Men aged 65–74 for lung cancer, (b) women aged 65–74 for diabetes, (c) men aged 45–64 for coronary heart disease,

Table 1 also presents standardized annual hospital-in-patient-days utilization for 1990, and projections for 1995. A comparison of the results in the two years for lung cancer demonstrates decreasing utilization for men and a stable pattern for women. For men in the age groups 45–64 and 65–74 we estimate downward trends in utilization (Fig. 1(a)). For diabetes downward trends prevail; this is most pronounced

FIG. 1. (*continued*) (d) women aged 75+ for stroke, (e) men aged 75+ for pneumonia, (f) men aged 65-74 for diabetes, (*continued*)

for women in the age groups 65-74 and 75+ (Fig. 1(b)). For young men and women with diabetes (mainly insulin-dependent diabetes mellitus, IDDM), we project a rather stable utilization with a slightly higher utilization estimated for 1995 than in 1990. Further, we estimate downward trends in utilization for coronary heart disease for all age groups (especially the 45-64 age group; Fig. 1(c)), whereas utilization patterns for stroke victims are fairly stable (Fig. 1(d)). In general, the projections of

FIG. 1. (continued) (g) boys aged 0–14 for pneumonia, and (h) women aged 65–74 for lung cancer.

utilization for pneumonia are slightly lower in 1995 than the 1990 levels. However, some time series demonstrate a positive or negative tendency (Fig. 1(e)). For all the diseases selected, the overall projections of standardized in-patient days for 1995 are lower than the levels observed in 1990.

The seasonal effect evident in SARIMA models with a nonzero D is illustrated in Figs 1(a) and (c). In addition, in models with a P of at least two, seasonality only slowly declines in the projections (Figs 1(f) and (g)). If the order of P is lower than two the seasonal pattern disappears very quickly (Fig. 1(h)).

Seasonality appears to be a very important factor influencing hospital-in-patient-days utilization. The effect is absent only for women with lung cancer. The pattern for men with lung cancer and for all patients with diabetes is characterized by a dip in utilization in December, followed immediately by a rise towards a peak in March (see Figs 2(a) and (b)). These findings agree with the notion of holiday periods causing relatively low utilization because of low staff capacity and patients postponing in-patient care. For female IDDM patients aged 0–14 there is no evidence of a December dip in utilization (Fig. 2(c)). Instead, for both this group and for coronary-heart-disease patients (Fig. 2(d)) the pattern is of a late-winter peak followed by a late-summer dip. For diabetes, this trend appears to reflect seasonal

FIG. 2. Projected standardized, monthly utilization of hospital in-patient days in 1995: (a) men aged 65–74 for lung cancer, (b) women aged 65–74 for diabetes, (c) girls aged 0–14 for diabetes, (d) men aged 45–64 for coronary heart disease, (e) women aged 75+ for stroke, and (f) boys aged 0–14 for pneumonia.

patterns in incidence [24, 25], whilst the pattern for coronary heart disease may be associated with seasonal mortality rates [26].

The seasonal pattern is most pronounced for stroke and pneumonia. In-patient utilization by stroke patients is up to one-third lower in December than in other months (Fig. 2(e)). For pneumonia, utilization is up to four times higher in late autumn and winter compared to midsummer (Fig. 2(f)), which reflects the usual seasonal epidemic of respiratory infections [27].

Figure 3 presents 95% confidence intervals for a number of projections. For Fig. 3(a) to (f) the intervals vary from near 0% to almost 100% around the projected levels.

Taking demographic effects into account, we estimate population-based projections for the overall utilization of hospital in-patient days in 1995 of 201 000 for lung cancer, 230 000 for diabetes, 832 000 for coronary heart disease, 685 000 for stroke,

Key: (▨) projection; (■) lower 95% confidence limit; and (□) upper 95% confidence limit.

FIG. 3. Projected standardized monthly utilization of hospital in-patient days in 1995 and the corresponding lower and upper 95% confidence limits: (a) women aged 65–74 for lung cancer, (b) men aged 65–74 for diabetes, (c) men aged 45–64 for coronary heart disease, (d) women aged 75+ for stroke, (e) men aged 65–74 for pneumonia and (f) men aged 75+ for pneumonia.

and 186 000 for pneumonia. Over the five-year period investigated we estimate that the changing demographic structure results in an additional in-patient-days utilization of 9% for lung cancer, 7% for diabetes, 10% for coronary heart disease, 8% for stroke, and 7% for pneumonia. Similar figures of the demographic impact on Dutch-health-care utilization and costs have been reported by others [28, 29]. Finally, the 1995 population-based in-patient utilization is projected to be below the 1990 level only for lung cancer and diabetes.

4. Discussion and conclusions

Our time-series analysis has demonstrated that for most sex and age groups disease-specific series for the utilization of hospital in-patient days can be adequately represented by SARIMA models. However, there are doubts about the adequacy of the models for some specific groups and diseases: men with lung cancer, all diabetes patients, and women with coronary heart disease or with stroke.

We have also found that the Portmanteau test is very sensitive to the size of M . For certain groups, such as men with lung cancer in the age groups 45–64 and 75+, a different choice of M would even have resulted in p -values below 0.10 (respectively, $M = 21$ and $M = 15$). As a further example, the poor Portmanteau test scores for women aged 75+ with coronary heart disease or stroke can be much improved by choosing M in the range 15–21, lowering the p -values down to 0.20 and 0.15. Only for diabetes is an insensitivity to the value of M apparent; representation of the diabetes series by SARIMA models remains inadequate.

Further analysis can be conducted by creating two utilization time series for discharges and for mean duration of stay (Fig. 4). The number of discharges acts as a proxy for the trend in the occurrence of disease, whilst the mean duration of stay provides an indicator of trends in care provision and efficiency; see, for example, [30]. The fact that the information on discharges is not patient based—one patient may account for several discharges in the data file—can disturb these interpretations [31]. We estimate that 55% of the total number of discharges for coronary heart disease in 1993 were for patients with one discharge in that year and 23% were readmissions [32]. However, if there is no significant change in clinical practice, for example by splitting up a long in-patient stay into two shorter ones, the possible bias we introduce in our analysis is likely to be only very small.

We find that projected decreases in hospital in-patient days for lung cancer and diabetes patients is associated with decreases in the mean duration of stay in 1980–90 (Fig. 4), as has also been demonstrated by Ruwaard *et al.* [10]. For pneumonia the reduction in the mean duration of stay outweighs the increase in discharges over the period. The same pattern exists for coronary heart disease and for stroke in the period 1980–85, whilst for stroke in the period 1985–90 the opposite trend of an increasing mean duration of stay and decreasing discharges is apparent.

There is limited information available on epidemiological developments for certain diseases. An epidemiological model for diabetes has been developed for The Netherlands, and some sampled data is available for incidence and prevalence [33]. The estimated increase in prevalence for the period 1980–90 is 28%, and a further increase of 13% for 1991–95 is expected (demographical developments account for half of the increase in both periods). This development appears to conflict with our SARIMA-model projection, although the discrepancy might be partially explained by the decrease in the mean duration of stay. But the epidemiological development is not in line with the trend in the number of discharges. One important factor influencing this pattern could be a shift from in-patient to out-patient treatment [34], since it is presumed to be cheaper [35] and more convenient for diabetic patients to start administering insulin in the latter setting.

FIG. 4. Indexed developments in annual standardized number of discharges, mean duration of stay per discharge, and utilization of hospital in-patient days (1980–1990; the base year for indexing is 1990): (a) lung cancer, (b) diabetes, (c) coronary heart disease, (d) stroke, and (e) pneumonia. Source, SIG, data processed by RIVM. (After, Ruwaard *et al.* [10].)

Results from models for both main diseases of the circulatory system have recently been published [36, 37]. For the period 1980–90 the standardized incidence and prevalence of coronary heart disease is estimated to have decreased, whereas we saw a contrasting increase for in-patient stays. This pattern has also been found in the USA [38]. For stroke, the decrease in the number of stays in 1985–90 is in line with an estimated decrease in incidence in the same period. These patterns clearly need further investigation.

Obviously, the projections of in-patient days would differ substantially if these were based on epidemiological developments rather than SARIMA modelling. (A projection based on epidemiological developments would be defined, reflecting the demand for in-patient days, assuming a constant sex- and age-specific *per-patient* utilization. In practice, this means that age- and sex-specific utilization of in-patient days, as registered in 1990, is multiplied by some factor of change for incidence or prevalence. For acute hospital care, incidence based is favoured (e.g. ICD 410 and stroke), whereas for chronic care prevalence based is favoured; for example, diabetes in a hospital or stroke in a nursing home.) Possibly, extrapolations of SARIMA models more closely reflect reality, since these take into account all the factors influencing the utilization of in-patient-days (for instance, shifts from in-patient to out-patient care, improved treatment, reductions in physical (bed) and budgetary capacity, increased productivity; see [39–41]).

We plan to extend our time-series analytical approach to other diseases which have a major impact on health-care-resource utilization, such as obstructive chronic lung diseases, arthrosis, dementia, and other types of cancer [42]. We also intend to extend the method to other health-care sectors, enabling comparison between settings, for example, acute versus long-term care for stroke [43].

In addition, an important issue concerns the nature of reductions in duration of stay and the downward effect this has on in-patient days. For acute myocardial infarction (ICD 410) Scitovsky showed that most of the decrease in duration of stay in the 1970s in the USA was due to a reduced utilization of care in regular wards, with a much lower reduction in intensive-care days [44]. Similarly, for diabetes the low intensive-care days will be shifted to out-patient facilities.

Of course our SARIMA approach has its limitations. Assumptions that recent trends will continue may be unrealistic and may lead to misleading results. For example, a continuing fall in the mean duration of stay for some diseases might be questioned. Availability of data for more recent and coming years will reveal this. More data would also enable us to extend the projection beyond the year 2000. Finally, there may be unforeseen events, such as the appearance of a new medical technology or changes in waiting-list management. Such events are not incorporated in our approach and would require construction of *several future scenarios* instead of *one* time-series extrapolation. Therefore it is important to design a complementary set-up for studying the scenario analytic approach to diseases [45, 46]. However, we may conclude that, despite the limitations, our projections are logical and reasonable illustrations of the probable short-term trend in in-patient-day utilization in Dutch hospitals.

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