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Evaluation of the health economic impact of the AO Foundation

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Abbreviations used (in alphabetical order):

AO	Arbeitsgemeinschaft für Osteosynthesefragen
AOCID	AO Clinical Investigation and Documentation
ARI	AO Research Institute
CHF	Swiss Francs
CMF	Cranio-maxillo-facial
CONS	Conservative fracture therapy
CPP	Clinical Priority Programm
DT	Decision tree
EDI	AO Educational Institute
GDP	Gross domestic product
HTA	Health Technology Assessment
LESD	Laboratory for Experimental Surgery Davos
LYG	Life years gained
ORIF	Open Reduction and Internal Fixation (in fracture care)
OS	Osteosynthesis (for fracture therapy)
PRO	Patient reported outcome
QALY	Quality adjusted life year
QOL	Quality of life
RfP	Request for Proposal
SSUV	Swiss SSUV accident insurer data base
VETcare	Veterinary care
WIG	Winterthur Institute of Health Economics
ZHAW	Zurich University of Applied Sciences (Zürcher Hochschule für Angewandte Wissenschaf-ten)

Management Summary

Background and aim of study

The project investigated the health economic impact of the AO Foundation in the last 60 years with particular focus on contributions in different areas, which are each responsible for impact, alone or in combination:

- Impact of **cultural change** (from conservative to surgical treatment based on new technology osteosynthesis)
- Impact of **education** to train surgeons applying more efficient and effective methods
- Impact of standardized surgical **methods and products**
- Impact of **research outcomes** that have been achieved over the time period surveyed
- Impact of the AO Foundation on **commercial investments** conducted

A methodological framework was developed to conceptualize and distinguish “input”, “activities”, “output”, “outcome” and “impact”. We assessed the overall impact over the past 60 years in five impact domains (Figure MS):

- Patient care
- Education
- Business
- Science
- Spine, CMF, VETcare

These five impact domains were treated as work packages during our study and will be named work packages (WP1 Patient care, WP2 Education, etc.) throughout the report.

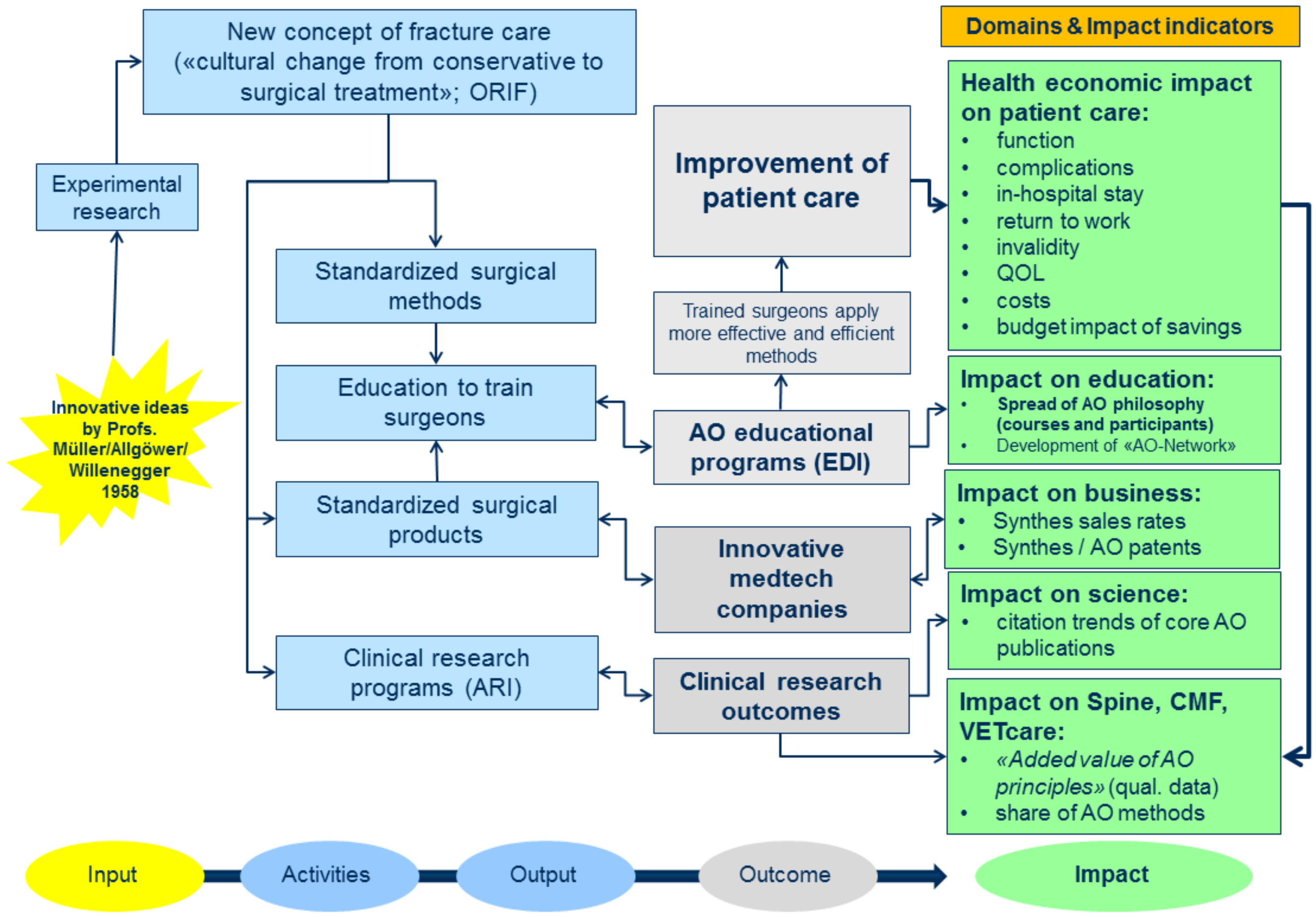

Figure MS-1: **Conceptual model with five impact domains and corresponding impact indicators**

Research questions

Based on the objectives of the impact evaluation and the methodological framework, the following research questions were addressed:

1. What is the impact of the technological innovation of osteosynthesis in fracture care?
2. What is the impact of the AO on the domains (medical) education, business and science?
3. Is there any added value of the AO principles on Spine, CMF, VETcare?

Methods

Design

We applied a mixed methods approach using quantitative and qualitative data.

Methods of WP1 Patient care

To estimate the impact of the technology osteosynthesis in fracture care over six decades (time span from its invention in 1958 to 2017), we presumed a (hypothetical) absence of this technology.

Design: We used a modelling approach with a decision tree (DT) to assess direct medical costs, indirect costs (also called productivity losses) and return to work rates for different treatment options. We compared osteosynthesis (OS) with conservative treatment (CONS) for fractures of three index bones (femur; tibia; radius). For our base case Switzerland, we used a bottom-up approach, as we had detailed data for many input variables. To extrapolate our results to other high income countries, we used a top-down approach and applied the findings from Switzerland to 16 high income countries taking country specific features into account (see below).

Data sources: We used claims data of the mandatory Swiss accident insurance scheme (Suva) and some private accident insurers (SSUV database), which include a working age population.

In addition, we used data from the Swiss MedStat database, which covers all inpatient treatments. In this database also patients beyond working age are documented (defined as age group ≥70 years in this database).

Population: We included the employed Swiss population (aged <65 years), as documented in the SSUV database. Non-employed persons in working age (e.g. students; persons with unpaid work at home) were excluded.

For femur fractures, we also included elderly patients ≥70 years. Proximal femur fractures of elderly persons beyond working age are a considerable and increasing disease burden for health care systems of high income countries. [1-3]

Included patients had a fracture of one of the three index bones as main diagnosis: femur, tibia and radius (for included ICD codes of proximal, shaft and distal fractures of index bones: Table A3.1). These three index bones were selected as they include frequent fracture locations of the upper and lower extremities and have specifically profited from OS innovations.

Patients with other main diagnoses and concomitant index fractures were excluded.

Intervention: Osteosynthesis (OS) of fractures of the three index bones (femur; tibia, radius).

Comparator: Conservative treatment (CONS) of fractures of the three index bones (femur; tibia, radius).

Outcome:

(1) Direct medical costs (for SSUV population <65 years; for the population aged ≥ 70 years only for proximal femur fractures)
(2) Indirect costs (for SSUV population <65 years)
(3) Years of life gained (YLG)

Direct medical costs (Swiss Francs; CHF) were derived using treatment costs as provided by the SSUV database or by 2015 Swiss tarifs. Indirect costs comprise intermediate absence from work, permanent absence from work without death, permanent absence from work due to death.

Observation period: Our analysis covers a time period of six decades from 1958 (founding of the AO) to 2017 (latest data available). We compared OS and CONS for each year and summed up possible increased costs or savings of all 60 years.

Selection of 17 high income countries: We defined a convenience sample of 17 countries to estimate the impact of OS on fracture care worldwide: 11 countries from Europe (including Switzerland), 2 from Northern-America and 4 from Asia/Pacific (Table MS-1).

Europe	
Switzerland	SUI
Germany*	GER
Austria	AUT
Belgium	BEL
Netherlands	NED
Luxemburg	LUX
United Kingdom	GBR
Denmark	DEN
Norway	NOR
Sweden	SWE
Finland	FIN
North-America	
United States	USA
Canada	CAN
Asia/Pacific	
Japan	JPN
Korea**	KOR
Australia	AUS
New Zealand	NZL

Table MS-1: **Sample of 17 high income countries for analysis.** *Federal Republic of Germany and German Democratic Republic combined for the time before 1989; **Korea only since 2000, when it became an OECD high income country.

We only included selected high income countries to have a group of countries that was comparable concerning economic conditions, medical technology penetration, population patterns and life style factors. We took the following four country specific features into account in our model: (1) population size; (2) health care expenditures; (3) gross domestic product per capita; (4) a country specific "technology penetration factor" to account for historical differences in the OS technology penetration speed compared to Switzerland (for the year 2000, technology penetration rate was set to 100% for all included countries).

With this approach, we finally derived an estimate of the accumulated difference in direct and indirect costs of fracture care with OS compared to CONS for nine index fractures in 17 high income countries over 60 years.

Analysis: We performed our analysis from a societal perspective and included direct and indirect costs.

The time horizon for extrapolation of future costs/savings was from injury to end of working age 65 for the SSUV population; and from injury to end of life for the femur fracture population aged ≥70 years.

Discounting: We used a fixed discount rate of 3% for indirect costs of the SSUV population. For example, if the mean age of femur shaft fractures in the SSUV population was 45 years, we discounted avoided productivity losses (i.e. productivity gains) of OS compared to CONS to the next 20 years until age 65 with a discount rate of 3%. Direct medical costs were not discounted, as they incur usually close to the time of fracture. In addition, we discounted the years of life gained in the elderly population (proximal femur fracture; age ≥70) using a fixed discount rate of 3%.

Currency and accounting for inflation: We applied 2015 Swiss costs for all modelled years (1958 to 2017; few historical cost data that were available went more or less hand in hand with the Health Component of the Swiss consumer price index over the last 60 years).

Sensitivity analyses: We performed a series of one-way sensitivity analyses on key parameters to assess the magnitude of influence on outcomes.

Methods of WP2 to WP5

For the WP2 Education, WP3 Impact on Business and WP4 Science we extracted data from hard copy documents and electronic databases and applied time series analyses.

For WP 5 Spine, CMF, VETcare, we evaluated with a more qualitative approach spill-over effects from each of the preceding work packages.

Results

Femur fractures: Key findings for the population age <65:

- Savings due to OS compared to CONS in patients with femur fractures (age <65) are CHF 131’000 per patient (direct and indirect costs) which is mainly due to savings of indirect costs (CHF 127’000).
- For the period 1958 to 2017, extrapolation of these savings to the modelled Swiss population (age <65) resulted in CHF 5 billion.
- For the period 1958 to 2017, extrapolation of total savings for femur fracture treatment in 17 high income countries (age <65) resulted in CHF 272 billion.
- The extrapolation to all 17 high income countries resulted in 2.5 million life years gained (about 2/3 of these life years are gained before age 65 and included in productivity gains, i.e. indirect cost savings)

Femur fractures: Key findings for the population age ≥70:

- For the period 1958 to 2017, extrapolation of savings in direct medical costs for treatment of proximal femur fractures in the modelled Swiss elderly population (age ≥70) resulted in CHF 1.1 billion.
- For the period 1958 to 2017, the extrapolation of these savings in direct medical costs (proximal femur fractures; age ≥70) to all 17 high income countries resulted in CHF 69 billion.
- For the period 1958 to 2017, extrapolation of the number of life years gained for treatment of proximal femur fractures in the Swiss population (age ≥70) resulted in 1.1 million life years gained.
- The extrapolation to all 17 high income countries resulted in 73 million life years gained.
-

Tibia fractures: Key findings for the population age <65:

- Savings due to OS compared to CONS in patients with tibia fractures (age <65) are CHF 104’000 per patient (direct and indirect costs) which is mainly due to savings of indirect costs (CHF 102’000).
- For the period 1958 to 2017, extrapolation of these savings to the modelled Swiss population with tibia fractures (age <65) resulted in CHF 9.8 billion.
- For the period 1958 to 2017, extrapolation of total savings for tibia fracture treatment in 17 high income countries (age <65) resulted in CHF 507 billion.
- The extrapolation to all 17 high income countries resulted in 2.1 million life years gained (about 2/3 of these life years are gained before age 65 and included in productivity gains, i.e. indirect cost savings)

Radius fractures: Key findings for the population age <65:

- Savings due to OS compared to CONS in patients with radius fractures (age <65) are CHF 13’700 per patient (higher direct costs: CHF +4’500; lower indirect costs: CHF -18’200).
- For the period 1958 to 2017, extrapolation of these savings to the modelled Swiss population with radius fractures (age <65) resulted in CHF 1.5 billion.
- For the period 1958 to 2017, extrapolation of total savings for radius fracture treatment in 17 high income countries (age <65) resulted in CHF 77 billion.

Summary of our sensitivity analyses:

We estimated savings of total costs due to OS of fractures of the three index bones over 60 years in the 17 selected high income countries of CHF 850 bn. (base case “best guess” at discount rate 3%; most conservative case in one-way sensitivity analyses: CHF 360 bn.; currency: 2015 Swiss Francs).

Results of WP2 Education

The AO's engagement in training and education is an essential reason for the worldwide acceptance of osteosynthesis and for the long-term success of the AO. The AO courses played an essential role in the training of surgeons willing to use the "AO technique", i.e. high quality osteosynthesis based on sound, standardized and empirically validated methods and procedures. However, the AO courses' impact went way beyond the immediate effects of knowledge transfer. Of equal importance were the networks between fellow surgeons that were built and fostered during such activities. Finally, the commercial success of the Synthes products was largely due to the AO courses where participants got acquainted with Synthes materials and tools and were introduced to new products directly from their peers. While not intentionally conceived as such, the AO courses not only turned out to enhance the AO's prestige and credibility, but also to promote the sale of Synthes products.

Our key findings:

- 65'000 surgeons were trained in the "Davos courses" from 1960 to 2016
- 580'000 surgeons were trained in worldwide courses outside Switzerland from 1965 to 2016
- 8'700 courses with about 20'000 teaching days were delivered in worldwide courses from 1965 to 2016
- 7'800 surgeons participated in fellowship programs from 1971 to 2017

Results of WP3 Impact on Business

Recognizing the need for appropriate materials, the AO got in contact with potential manufacturers right in its beginnings and supervised the production, marketing and sales of the osteosynthesis products it developed. The AO's special relationship between doctors and industry not only led to the development and successful promotion and sales of osteosynthesis materials, it also generated a steady stream of royalty payments that the AO invested in education, documentation and research. However, Synthes sales increased exponentially over time and generated a large, successful, international business on their own. A dynamic, which finally led to the separation between the AO and its business counterpart, the Synthes AG Chur. With the sale of the Synthes brand and the AO patents to Synthes Inc. in 2006, the AO has become an exclusively professional and educational organization with no more direct relationships with Synthes producers. However, ties to

Synthes Inc. and, later on, Johnson and Johnson DePuy Synthes remained close and found a formal basis in cooperation agreements in order to carry on joint work in education and innovation in trauma care and related fields.

Our key findings:

- Synthes sales of all producers at royalty base price 1961 to 2005 sum up to CHF 11,6 bn.
- Synthes US/Synthes Inc. sales at final prices from 1975 to 2016 sum up to CHF 54.5 bn.

Results of WP4 Science

AO Research has been one of the founding pillars for the AO since the beginning and the impact of AO science is manifold. One of the main products of AO research was to generate patents and improve surgical processes. These indirect impacts of science are treated in the WP Education (WP2) and WP Business of Medtech industry (WP3). Aside from indirect impacts AO science also influences other researchers via manuscripts, collaborations, by taking an active part in medical associations or by creating or supporting platforms for scientific exchange. Furthermore, the AO invests substantial funds to further research in- and outside its walls. Therefore, we measured the impact of the AO on science in four dimensions: Citation trends of core publications, internal and external funding by the AO, collaborations in studies or relationships to universities, and fostering the scientific community.

Our key findings:

- Several early AO books and journal papers are still relevant for research community today
- 25’535 total citations for the 2 most cited core papers since 1996
- 9 core papers in the top 1% of highly cited papers in their field in the past 9 years
- A growing number of papers in journals with IFs above 4.0 from 2007 to 2016
- CHF 289.6 Mio of funding for LESD/ARI from 1960 to 2016 and CHF 28.9 Mio of funding for CID from 2013 to 2016
- 327 collaborations within studies and with universities in the past 19 years.

- Yearly scientific conference and publication of a scientific journal with an impact factor above 4.0 since its first classification

Results of WP5 Spine, CMF, VETcare

Relevant spill-over effects were found for Spine, CMF and VETcare in different domains.

Our findings in the domains “Impact on Business”, “Impact on Education” and “Impact on Science” provide some few data about sales rates of OS products, education of clinical methods and progress in science related to spine and CMF care.

Concerning patient care, this can be seen as an indicator for the patient volume and the progress that has been made by these well-established treatment options. Based on those figures, a relevant impact of the AO innovations on patient care can be assumed also in the spine and CMF domain. We were not able to formally assess costs. The spine and CMF patients of the Swiss working age population are a mix of patients treated with OS and those treated conservatively. In the absence of detailed figures for the ratio of patients treated with OS, the health economic impact of OS for the health care system can only be assumed.

Similar savings due to OS may have been realised per patient in spine and CMF care as for the three index bones, when an indication for OS is given. This may be especially the case for cervical spine trauma patients, where total costs are still high in the era of OS (mean direct and indirect costs per patient: CHF 71’000).

Discussion

Strengths and limitations of our study

We used real world patient care data from a large accident insurance company, to describe resource use and costs for state-of-the art fracture care of three index bones in a high-income country (Switzerland). We had also access to historical treatment data for Switzer-land (partly form 1958; mostly from 1980 up to 2015). Furthermore, we modelled different fracture locations for each of the index bones separately, to account for different clinical courses. In addition, we used country specific data for all included 17 high-income countries for population size, health care expenditures, national wages and life expectancy.

In summary, our results of impact on patient care represent conservative estimates as we applied conservative assumptions for input parameters of our model. For example:

- We included only cases with a fracture of an index bone as main diagnosis.
- Historical fracture care data and costs, sometimes as early as 1960, were only available for patients younger than 65 years.
- Possible effects in other (excluded) high- or middle-income countries (e.g. BRIC-countries: Brazil, Russia, India, China) are not covered.

Our modelling approach of WP1 (impact on patient care) has several limitations as it is based on critical assumptions. For example:

- The availability of historical cost data in the SSUV data base was sometimes scarce and we assumed 2015 Swiss prices for all years. We validated this approach by inflating retrieved (lower) historic prices to (higher) 2017 Swiss prices via the Health Component of the Swiss consumer price index from 1958 to 2015.
- Coding of diagnoses changed over decades (ICD-8, ICD-9, ICD-10) and calculation mode of some cost elements showed some variation over 60 years (e.g. payments for days off work after injury).
- The workforce of high-income countries has changed over time (changing sector mix with decreasing fraction of blue collar and increasing fraction of white collar workers). While this has implications for injury patterns during work time, which is included in the SSUV data, it has also implications for calculation of invalidity rates and success of occupational redeployment. To take this into account in our sensitivity analysis, we have varied invalidity rates towards lower values reflecting a higher degree of white collar workers.
- We used fracture specific cost data for Switzerland, but no such national data were available in the same granularity for the other high-income countries.
- From the year 2000 onwards we assumed a technology penetration rate of 100% in all included high income countries. This may not always and in all regions be the case, as studies about regional variations in health care systems have shown empirically.

- In addition, complication rates may differ substantially depending on regional case mix and surgeon case load. We had no specific data to take these factors into account in our study.
- For some country features, we assumed similar conditions over time for all included high-income countries as in Switzerland (i.e. change of age structure of population; epidemiology of changes in fracture incidence over time).
- Organisational and financial responsibilities in a health care system may differ across countries. For example, our approach is derived from the perspective of a social insurance based health care system. Such a perspective is not valid for the whole observation period for some countries (e.g. mostly private health insurance system of the USA, until the Affordable Care Act in 2012).

The range of savings of total costs due to OS of fractures of the three index bones is estimated in a range between CHF 300 to 800 bn over 60 years in the 17 selected high income countries (currency: 2015 Swiss Francs). This wide range shows the amount of uncertainty in our results, as our estimation is based on several consecutive assumptions. However, even the most conservative estimation of CHF 300 bn of savings in direct and indirect costs over 60 years are substantial.

Our impact assessment for the remaining work packages (Impact on Education; Impact on Business; Impact on Science) has also specific methodological limitations, for example:

Impact on Education:

- More recently, online materials such as videos, online courses, and, in particular, the AO Surgery Reference, have become very important resources for surgeons performing osteosynthesis and for fracture care in general. However, as we had only limited data on the use of these resources over time, we refrained from an in depth analysis.

Impact on Business:

- We had difficulties to find sales figures of products directly related to the AO over time. Nevertheless, we are in the position to give an account of the detailed development of Synthes sales over the past 60 years.
- Because we have no data on the various production sites of the Synthes producers, on imports and exports, nor on the value added at a particular location, it was not possible to estimate a specific regional economic impact of the Synthes production.

Impact on Science:

- The AO does impact the science community in all their fields of research. However, because of its thematic breadth from basic research over clinical research to development of new techniques and patent deposition, it is difficult to cross-validate our results by comparing the AO science departments to other institutions such as universities, university clinics or to R&D departments of firms.
- In addition, citation-based measures are only an indicator of impact and represent a researcher-based view.

Significance of impact on patient care

The potential net benefit of OS for fractures in the three index bones in 17 high income countries over 60 years is CHF 855 bn (base case; population age <65; 3% discount rate; in 2015 Swiss Francs).

To break our figures down, we have made some comparisons.

In terms of excess deaths avoided, the annual impact of osteosynthesis on proximal femur fracture care in the US is in a similar dimension as the annual impact of antihypertensive care in the US (osteosynthesis: 2’600 lifes saved [population age: <65 years] plus 126’000 lifes saved [population age: ≥70 years]; antihypertensive drugs: 86’000 lifes saved [population age: 30-79 years]).

For comparison of cost savings, we used our combined estimates (femur, tibia and radius fractures; all locations; direct and indirect costs; population age <65 years). The impact of osteosynthesis in the US in the year 2002 is again in a similar dimension as the annual impact of antihypertensive care in the US (osteosynthesis: 14.0 bn US$ saved; antihypertensive drugs: coronary heart disease [CHD]: 5.8 bn US$ saved; cerebrovascular disease [CVD]: 10.7 bn US$ saved; population age: 30-79 years). However, the annual savings due to antihypertensive drug in the US may be substantially underestimated in our comparison, as no indirect costs were included.

A tabulation of savings compared to the GDP may also be useful. The estimated cost savings for osteosynthesis and for antihypertensive drugs are in a comparable range when compared with the GDP of some example countries (antihypertensive drugs for CHD or CVD: USA 0.05 to 0.09% of GDP in 2002; OS for fractures: USA, Switzerland and Germany: 0.06% to 0.08% of GDP in 2016).

Synergistic effect of education, business and science

The three domains education, business and science have been treated separately in our report. However, since the beginning of the AO these three domains mutually enriched and reinforced one another. Basic results from science were needed to further the acceptance of the osteosynthesis technique among peers without which neither education nor business would have developed as shown in this study. Yet, only the closely-knit ties developed in education and the closeness to clinical work could also develop the knowledge and educated manpower that were the basis for further developments in science and the demand for the AO tool set which furthered business.

This interplay between these three domains was not a result of pure chance. It has been designed by the funders of the AO quite from the beginning. Urs Heim (2012) is citing Maurice Müller et. al. by mentioning the four pillars of the AO as being: Instrumentation, Research, Documentation and Teaching. Even though we treated documentation as part of research in our report, we believe, that only the synergistic effect of these domains could generate the impact detected in our study. The combined approach chosen by the funders lead to an overall impact that each domain alone could not have yielded by itself.

Conclusions

Based on the data available in this report, the technology of osteosynthesis had a significant impact on patient care after bone fractures over the last 60 years.

Improved functional results with higher return to work rates, as well as decreased mortality rates after long bone fractures had a dramatic impact: Osteosynthesis lead to significant productivity gains for society and saved a substantial amount of life years.

This impact was multiplied by the interdependence of three additional factors: The structured education of numerous surgeons to apply this technology, the rise of a Medtech industry in orthopaedics and the stepwise development of the scientific knowledge base of surgical fracture care, as assessed in our report. This virtuous cycle enabled a spread of this technology to many countries word wide.

Thus, osteosynthesis developed to the state of the art for treatment of a wide range of fracture types and has increased value of health care.

1 Background and aim of the impact evaluation

The AO Foundation is a medically guided non-profit organization led by an international group of surgeons specialized in the treatment of trauma and disorders of the musculoskeletal system. [4,5]

The AO (Arbeitsgemeinschaft für Osteosynthesefragen) was established almost 60 years ago to improve patient care in musculoskeletal disorders. It was a time where a trauma treatment would consist of cast and extension treatment and patients would stay in hospital for an extended period of time (as today in low income countries).[5]

Together with some industry representatives, a number of Swiss surgeons (Prof. Dr .med. M. Müller et al.) developed a new method to treat patients including the internal fixation methods. [5]

This was the beginning of the Medical Device Industry in the clinical field of traumatology/orthopedics. The objectives were to improve patient outcome, reduce the patients' pain but also to reduce time in hospital and time before the patient would be back at work. Four main principles of fracture care were established to reach these aims: anatomical reduction, stable fixation, preservation of blood supply and early mobilization. The founder's objectives even at that time included a health economic aspect.

Since that time the AO Foundation developed into a large organization. In the year 2015 it had around 280 employees, over 1'000 faculty and up to 20'000 members. With over 700 courses it trained over 50'000 surgeons globally.

The AO Foundation wanted to have a scientific look at the impact of AO Foundation over the last 60 years and make it known to a wider public. Several books exist but they are more anecdotal to historical developments and people as well as medical developments.

The Winterthur Institute of Health Economics (WIG), Zurich University of Applied Sciences, won the bidding process to evaluate the health economic impact of the AO Foundation in the last 60 years.

2 General methods of impact evaluation

2.1 Objective

The project investigated the health economic impact of the AO Foundation in the last 60 years with particular focus on contributions in different areas, which are each responsible for impact, alone or in combination:

- Impact of **cultural change** (from conservative to surgical treatment)
- Impact of **education** to train surgeons applying more efficient and effective methods
- Impact of standardized surgical **methods and products**
- Impact of **research outcomes** that have been achieved over the time period surveyed

In addition, the Medtech business area was part of the evaluation:

- Impact of the AO Foundation on **commercial investments** conducted

For each of these areas above, outcome measures were derived for measurement of the impact of the AO Foundation in several domains.

2.2 Methodological framework

A methodological framework was developed to conceptualize and distinguish “input”, “activities”, “output”, “outcome” and “impact”. Such a framework is essential to correctly formulate and address relevant research questions.[6] The conceptual model for the AO impact evaluation is depicted in Figure 2.1. We assessed the overall impact over the past 60 years in five impact domains:

- Patient care
- Education
- Business
- Science
- Spine, CMF, VETcare

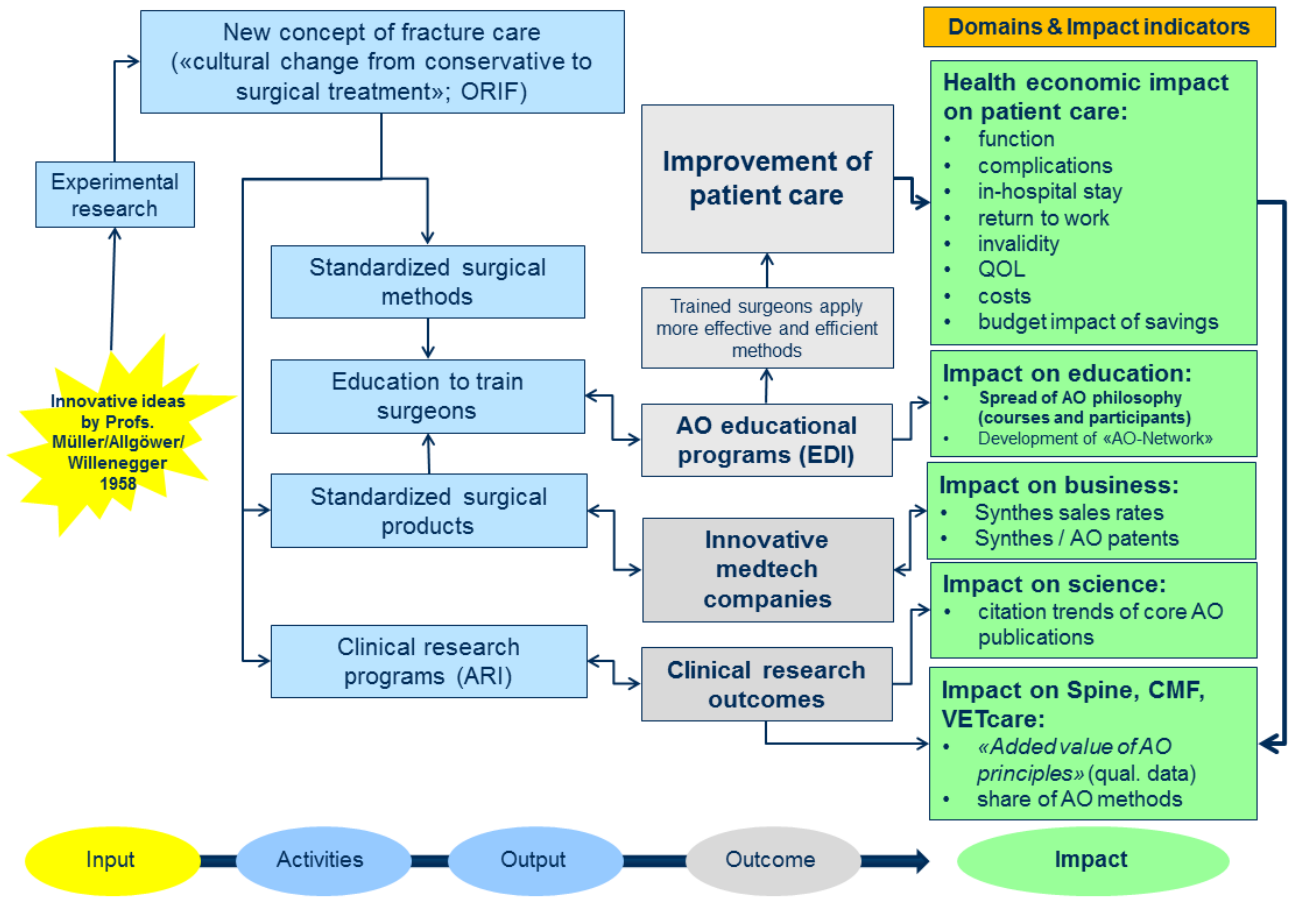

Figure 2.1: **Conceptual model with five impact domains and corresponding impact indicators**

2.3 Research questions

Based on the objectives of the impact evaluation and the methodological framework, the following research questions were addressed:

4. What is the impact of the technological innovation of osteosynthesis in fracture care?
5. What is the impact of the AO on the domains (medical) education, business and science?
6. Is there any added value of the AO principles on Spine, CMF, VETcare?

2.4 Design

We applied a mixed methods approach using quantitative and qualitative data (Table 2.1).

This approach comprised:

- literature searches
- analysis of databases with quantitative data
- health-economic modelling to estimate effects over time
- interviews with key stakeholders and clinicians
- interviews with persons, who have been witnesses of the development of the AO Foundation over decades and had insight into the complex interaction of different contributions made (for example between structured education of surgeons and improved clinical care).
- evidence synthesis

We report the results for each of the principal domains “patients care”, “education”, “business” and “science” separately as work packages (WP 1 to 4). Results concerning “Spine-, CMF- and VETcare” (work package, WP 5) have been assigned to each of these principal domains.

Domain	**Alternatives compared**	**Time periods**	**analysis**	**Data sources**	**impact**	**Impact indicators** (examples)
Patient care (work package 1)	Osteosynthesis vs. conservative approach	1958-2017	Quantitative	Literature searches Medical databases Cost data of accident insurances	Health economic impact	Difference in return to work rates Difference in costs (direct medical costs and indirect costs [production losses]) Life years gained (LYG)
Education (work package 2)	---	1958-2017	Quantitative; time series analysis	AO EDI annual reports	Acceptance of education Diffusion of educational approach	Number of AO courses over time per country Number of AO course participants over time per country
Business (work package 3)	---	1958-2017	Quantitative; time series analysis	Business reports of Medtech companies Annual reports	Sales rates of AO- and Synthes products	Sales volume over time
Science (work package 4)	---	1958-2017	Quantitative time series analysis Qualitative	ISI web of science Interviews	Citation of core AO publications Scientific networking	Citation rates of core publications Amount of AO-internal and AO-external research funding Number of scientific collaborations with academic partners world-wide
Spine, CMF, VETcare (work package 5)	(Osteosynthesis vs. conservative)	---	Quantitative Qualitative	Public data bases Business reports of Medtech companies Interviews	Introduced AO methods Introduced AO educational approaches	Narrative estimation of impact on Spine and CMF patient care Narrative estimation of impact on education, business and science in Spine, CMF and VET-care

Table2.1: **Overview over domains and applied methods for impact evaluation.**

2.5 Methodological and scientific advice

A steering committee was established in advance and provided methodological and scientific advice (the names of the experts of the Steering Committee are documented in the Acknowledgement section).

This committee comprised experts, who had intimate knowledge about the historical development of the AO, as such, as well as about the spread of the osteosynthesis technology over time and the evolvement of educational, business and scientific issues. In addition, management, medical, health-economic and epidemiologic expertise was covered by the committee.

3 Impact on patient care (WP1)

3.1 Methodological approach of this work package

To estimate the impact of osteosynthesis in fracture care over six decades (time span from its invention in 1958 to 2017), we presumed a (hypothetical) absence of this technology. This strategy has been used by other research groups.[7 8-10]

It is important to note, that for the impact on patient care we did not directly evaluate the impact of the AO on patient care but the impact of the technology of osteosynthesis as such. We did this for two reasons: (1) in the absence of AO, the technology of osteosynthesis may have likely been developed further by someone else during the last 60 years and (2) osteosynthesis methods and technologies have quickly spread over the world with many different products being used today, of which some have not originally been developed by the AO or its related medtech producers.

In contrast, the work packages “education”, “business” and “science” have a direct connotation with the AO.

Design: We used a modelling approach with a decision tree (DT) to assess direct medical costs, indirect costs (also called productivity losses) and return to work rates for different treatment options. We compared osteosynthesis (OS) with conservative treatment (CONS) for fractures of three index bones (femur; tibia; radius). For our base case Switzerland, we used a **bottom-up approach**, as we had detailed data for many input variables. To extrapolate our results to other high income countries, we used a **top-down approach** and applied the findings from Switzerland to these countries taking country specific features into account (see below).

Data sources: We used claims data of the mandatory Swiss accident insurance scheme (Suva) and some private accident insurers (SSUV database). This database covers about 60% of the Swiss population. Extrapolation of the case load to the full Swiss population is also possible.

To understand the institutional context of this database, one needs to know that there are two independent social insurance systems for health care in Switzerland. [11] First, there is compulsory health insurance that is compulsory for all inhabitants. Second, there is an accident insurance that is compulsory for all people in salaried employment. For others, such as the elderly, children, students or the self-employed, their health insurer also covers the costs of medical treatment in the case of accidents via an additional accident insurance. Accident insurance for the employed, however, has more generous benefits than health insurance. For instance, it also covers loss of working hours. The two parallel systems have evolved historically. The compulsory accident insurance scheme is operated by one large national insurance company, SUVA, with a partial monopoly for the employees in the manufacturing sector and several private insurance companies that compete for employees not covered by SUVA, e.g. almost the whole service sector. [11]

Both accident insurance groups contribute to the SSUV-database. This database contains direct medical costs for acute fracture treatment and rehabilitation (derived by number of used resource units multiplied with current Swiss prices). In addition, indirect costs due to production losses can be calculated. Production losses include absenteeism, permanent disability and premature death.

In addition, we used data from the Swiss MedStat database which covers all inpatient treatments. In this database also patients beyond working age are documented: For example, all patients aged ≥70 years with femur fractures and inpatient treatment can be identified for specific treatment years. As age groups in the Medstat database are grouped in fixed age classes of “40 to 69” and “70+”, we were not able to include patients from 65 to 69 years for analysis of patients beyond working age.

Population: We included the employed Swiss population (aged <65 years), as documented in the SSUV database. Non-employed persons in working age (e.g. students; persons with unpaid work at home) were excluded.

For femur fractures, we also included elderly patients ≥70 years. Proximal femur fractures of elderly persons beyond working age are a considerable and increasing disease burden for health care systems of high income countries. [1,2,12]

Included patients had a fracture of one of the three index bones as main diagnosis: femur, tibia and radius (for included ICD codes of proximal, shaft and distal fractures of index bones: Table A3.1). These three index bones were selected as they include frequent fracture locations of the upper and lower extremities and have specifically profited from AO innovations.

Patients with other main diagnoses and concomitant index fractures were excluded. For example, patients with craniocerebral injury as main diagnosis and an additional femur fracture were excluded, to avoid contamination of health-economic effects of the main diagnosis on the effect of OS on femur fractures.

Intervention: Osteosynthesis (OS) of fractures of the three index bones (femur; tibia, radius).

Comparator: Conservative treatment (CONS) of fractures of the three index bones (femur; tibia, radius).

Outcome:

(1) Direct medical costs (for SSUV population <65 years; for the population aged ≥ 70 years only for proximal femur fractures);
(2) Indirect costs (for SSUV population <65 years);
(3) Years of life gained (YLG)

Direct medical costs (Swiss Francs; CHF) were derived using treatment costs as provided by the SSUV data base or by 2015 Swiss tarrifs.

Indirect costs comprise

i. intermediate absence from work (calculated as number of months off work multiplied by 2015 median Swiss monthly wages of the same age group)
ii. permanent absence from work without death (number of months with 100% disability pensions before age 65 multiplied by monthly wages)
iii. permanent absence from work due to death (number of years lost due to premature death before age 65 multiplied by annual wages)

Improved mortality is expressed in our analysis in two ways:

- For patients aged <65: via productivity gains due to less premature death before age 65 (number of years of life gained, LYG, from fracture until end of life expectancy for this population group is also provided, but not used for calculation of indirect costs)
- For the population ≥70 years: via the number of life years gained (LYG)

Observation period: Our analysis covers a time period of six decades from 1958 (founding of the AO) to 2017 (latest data available). We compared OS and CONS for each year and summed up possible increased costs or savings of all 60 years.

Bottom up approach for Switzerland:

For each of the three index bones we modelled direct and indirect costs for proximal, shaft and distal fractures to take the diversity of the clinical course into account. Thus, we fed nine decision trees with fracture specific cost data and probabilities for either osteosynthesis or conservative treatment.

The structure of the decision tree (DT) was reviewed in advance by our scientific advisory board and amended as needed. The DT is a pragmatic simplification of fracture care and comprises three stages, for OS and CONS, alike (Figure A3.1):

- stage 1 (primary intervention: OS or CONS);
- stage 2 (fracture healing: “without bone related complications” or “with bone related complications”);
- stage 3 (venous thromboembolism [VTE], as an indicator for all non-bone related complications: “VTE no” or “VTE yes”).

For stage 2, complications of OS were defined as device infection, device dislocation and non-union. Complications of CONS were defined as non-union and mal-union. For stage 3, venous thromboembolism includes deep vein thrombosis and pulmonary embolism.

Transition probabilities between the different stages were derived from the SSUV database, from the literature or from expert opinion. Expected direct and expected indirect costs were modelled for each year. Finally, we could compare expected direct and indirect costs of each of the 9 index fractures over a period of six decades.

The number of life years gained in the femur fracture population aged ≥70 was calculated as follows: The difference in mortality rates (CONS minus OS) was multiplied with the time interval between mean age at the time of fracture and expected age of death in the general population in a given year in Switzerland.

Top down approach for additional 16 high income countries:

After consulting our expert group, we defined a convenience sample of 17 countries to estimate the impact of OS on fracture care worldwide: 11 countries from Europe (including Switzerland), 2 from Northern-America and 4 from Asia/Pacific (Table 3.1).

Europe	
Switzerland	SUI
Germany*	GER
Austria	AUT
Belgium	BEL
Netherlands	NED
Luxemburg	LUX
United Kingdom	GBR
Denmark	DEN
Norway	NOR
Sweden	SWE
Finland	FIN
North-America	
United States	USA
Canada	CAN
Asia/Pacific	
Japan	JPN
Korea**	KOR
Australia	AUS
New Zealand	NZL

Table 3.1: **Sample of 17 high income countries for analysis.** *Federal Republic of Germany and German Democratic Republic combined for the time before 1989; **Korea only since 2000, when it became a OECD high income country.

We only included selected high income countries to have a group of countries that was comparable concerning economic conditions, medical technology penetration, population patterns and life style factors. Using a top down approach, we then applied the results of the 9 index fractures from our Swiss base case to each of the 16 other high income countries. In total, we made 144 international extrapolations (9 index fractures in 16 countries) taking the following four country specific features into account:

(1) population size (as a proxy for case load);
(2) health care expenditures (PPP adjusted in US $; as a proxy for country specific prices in health care, affecting direct medical costs);
(3) gross domestic product per capita (PPP adjusted in US $; as a proxy for country specific wage levels, affecting indirect costs).
(4) a country specific "technology penetration factor" to account for historical differences in the OS technology penetration speed compared to Switzerland. This factor was estimated based on historical knowledge of interviewees, as well as on sales rates of Synthes products and the AO's local educational activities (GER, AUT: 5 years delay; other included European countries: 10 years delay; included Northern-America and Asia/Pacific countries: 25 years delay; for the year 2000, technology penetration rate was set to 100% for all included countries).

An overview over country specific features for calculating each of the four factors is given in the Appendix (Table A3.4). With this approach, we finally derived an estimate of the accumulated difference in direct and indirect costs of fracture care with OS compared to CONS for nine index fractures in 17 high income countries over 60 years.

Analysis:

We performed our analysis from a societal perspective and included direct and indirect costs. We could not rely on intangible cost data (e.g. utilities derived from Swiss quality of life data).

The time horizon for extrapolation of future costs/savings was from injury to end of working age 65 for the SSUV population; and from injury to end of life for the femur fracture population aged ≥70 years.

Discounting: We used a fixed discount rate of 3% for indirect costs of the SSUV population. [13] For example, if the mean age of femur shaft fractures in the SSUV population was 45 years, we discounted avoided productivity losses (i.e. productivity gains) of OS compared to CONS to the next 20 years until age 65 with a discount rate of 3%. We assumed productivity gains to be divided evenly over the 20 year time period. Direct medical costs were not discounted, as they incur usually close to the time of fracture.

In addition, we discounted the life years gained in the elderly population (proximal femur fracture; age ≥70) using a fixed discount rate of 3%. This approach takes into account that a life year gained in the present is perceived as of higher value than a life year gained in the future, let’s say in 5 years.

Currency and accounting for inflation: Data of historical costs in fracture care was scarce. We applied 2015 Swiss costs for all modelled years (1958 to 2017; inflation rate from 2015 to 2017 in Switzerland is negligible). The rationale behind this approach was that the few historical cost data that were available went more or less hand in hand with the Health Component of the Swiss consumer price index over the last 60 years (Figure A3.2).

Sensitivity analyses: We performed a series of one-way sensitivity analyses on key parameters to assess the magnitude of influence on cost outcomes, as well as on life years gained:

We varied discount rates for future cost savings and life years gained (base case: 3%; variations: 0% and 6%; using the same discount rate for cost savings and patient benefit).

We varied assumed invalidity rate for patients with CONS and a complication at stage 2 (mal-union; non-union) for their remaining time on the working market until age 65:

- For Femur fractures and for tibia fractures: base case (100% invalidity, variations: 80%, 60%)
- For radius fractures (base case: 20% invalidity, variations: 15% and 10%)

We varied the ratio between Swiss wages and the wages of the other 16 high income countries. With this sensitivity analysis we took into account that the relationship of wages may vary over time between countries depending on business cycles or regional economic problems:

- The GDP per person ratio (i.e. Swiss GDP per person / country X GDP per person), which was calculated using OECD data, was multiplied by 0.9 and by 0.8 (base case = 1). Thus, we increased the difference between the Swiss wages and the international wages. With this approach we created a more conservative estimate of savings in the other 16 high income countries.

3.2 Results

3.2.1 Femur fractures

Key findings for the population age <65:

- Savings due to OS compared to CONS in patients with femur fractures (age <65) are CHF 131'000 per patient (direct and indirect costs) which is mainly due to savings of indirect costs (CHF 127'000).
- For the period 1958 to 2017, extrapolation of these savings to the modelled Swiss population (age <65) resulted in CHF 5 billion.
- For the period 1958 to 2017, extrapolation of total savings for femur fracture treatment in 17 high income countries (age <65) resulted in CHF 272 billion.
- The extrapolation to all 17 high income countries resulted in 2.5 million life years gained (about 2/3 of these life years are gained before age 65 and included in productivity gains, i.e. indirect cost savings)

Key findings for the population age ≥70:

- For the period 1958 to 2017, extrapolation of savings in direct medical costs for treatment of proximal femur fractures in the modelled Swiss elderly population (age ≥70) resulted in CHF 1.1 billion.
- For the period 1958 to 2017, the extrapolation of these savings in direct medical costs (proximal femur fractures; age ≥70) to all 17 high income countries resulted in CHF 69 billion.
- For the period 1958 to 2017, extrapolation of the number of life years gained for treatment of proximal femur fractures in the Swiss population (age ≥70) resulted in 0.9 million life years gained.
- The extrapolation to all 17 high income countries resulted in 73 million life years gained.

Included population

Baseline data of our modelled population for femur fractures in Switzerland are depicted in Table 3.2 (working age population; age <65) and in Table 3.3 (elderly population; age ≥70).

	Femur proximal	Femur shaft	Femur distal	total
n (2011)	630	171	515	1316
n (total 1958 to 2017)	29085	23818	19456	72360
age (mean) at injury	51.8	33.6	33.5	
sex ratio (female)	0.31	0.32	0.18	
time span to age 65	12.94	31.08	31.32	
modelled person years	376366	740263	609374	1726004

Table 3.2: **Baseline data of working age population with femur fractures (SSUV population; age <65 years) as used for the estimation of direct and indirect costs.**

	Femur proximal
n (2011)	12200
n (total 1958 to 2017)	507550
age (mean) at injury	75.5
life expectancy	87
time span to exp. death	11.5
modelled person years	5836825

Table 3.3: **Baseline data of elderly population with femur fractures (age ≥70 years) as used for the estimation of direct and life years gained.**

In the working age population, we estimated 72’360 femur fracture cases (all locations) from 1958 to 2017 with over 1.7 Mio modelled person years.

In the elderly population (age ≥70), we estimated 507’550 proximal femur fracture cases from 1958 to 2017 with over 5.8 Mio modelled person years.

Results of working age population (age <65)

In patients with femur fractures, average direct medical costs in Switzerland in 2015 are one fifth lower for OS (CHF 19’600) compared to CONS treatment (CHF 24’200). While the acute care (hospital) costs for OS are higher compared to CONS treatment, a longer rehabilitation period for patients with conservative treatment finally leads to higher direct medical costs in this group according to our model assumptions (Table 3.4).

The difference for indirect costs is even more pronounced. Average indirect costs in Switzerland are only one fifth for OS (CHF 31’000) compared to CONS treatment (CHF

158’000) in this patient group. The main reason is, that with OS, patients have a shorter period of absence from work compared to CONS and higher return to work rates. In addition, lower mortality rates (OS: 0.3%; CONS: 3%) lead to decreased productivity losses due to premature death before age 65.

In summary, savings due to OS compared to CONS in patients with femur fractures in this age group are CHF 131’000 per patient which is mainly due to savings of indirect costs (CHF 127’000).

anatomic localisation of fracture	YEAR	AO/OTA	treatment	exp cost direct	exp cost indirect	exp cost total
Femur prox	2015	31-xx	OP	21349	28527	49'877
	2015		CONS	24202	111637	135'839
Femur dia (shaft)	2015	32-xx	OP	19430	52792	72'222
	2015		CONS	24202	204558	228'760
Femur dist	2015	33-xx	OP	17638	24856	42'493
	2015		CONS	24202	196671	220'873
Femur total costs (CHF weighted average; per patient)		31-33	OP	19652	30642	50'294
			CONS	24202	157620	181'822
Difference in total costs Femur (CHF per patient: CONS-OP)		31-33		**4550**	**126978**	**131528**

Table 3.4: **Expected direct and indirect costs of femur fractures (working age population; age <65) in Switzerland.** Costs are in 2015 Swiss Francs (CHF). Femur total costs are weighted for relative frequency of femur fracture locations.

The co-occurrence of higher return-to work rates and lower direct and indirect costs makes OS a clearly dominant intervention compared to CONS in this patient group (Figure 3.1; example for femur shaft fracture).

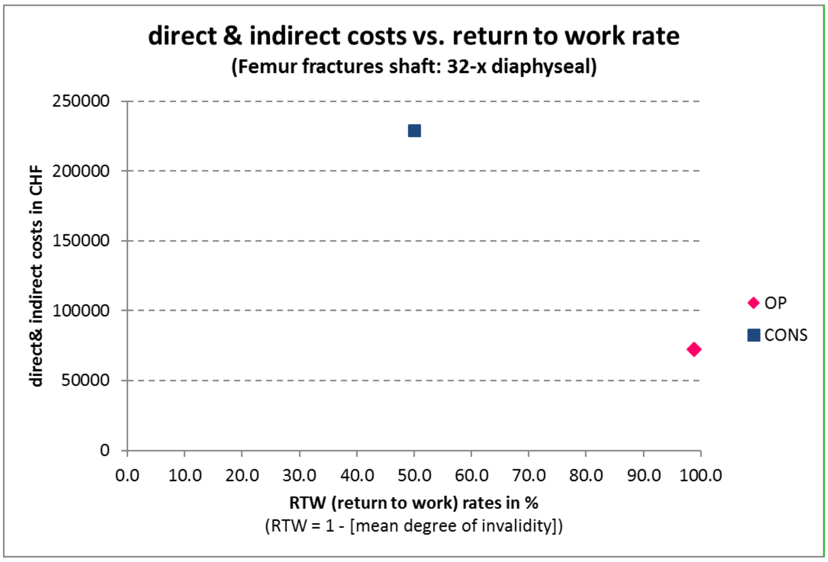

Figure 3.1: **Cost-effectiveness plot of OS vs. CONS in patients with femur shaft fractures.** Patient benefit (return to work rate) is depicted against total costs (i.e. direct plus indirect costs). Costs are in 2015 Swiss Francs (CHF).

Annual savings in total costs for femur fracture treatment due to osteosynthesis increased from 1958 to 2017, depending on changes in technology penetration and epidemiology of fractures (Figure 3.2; example for distal femur fractures).

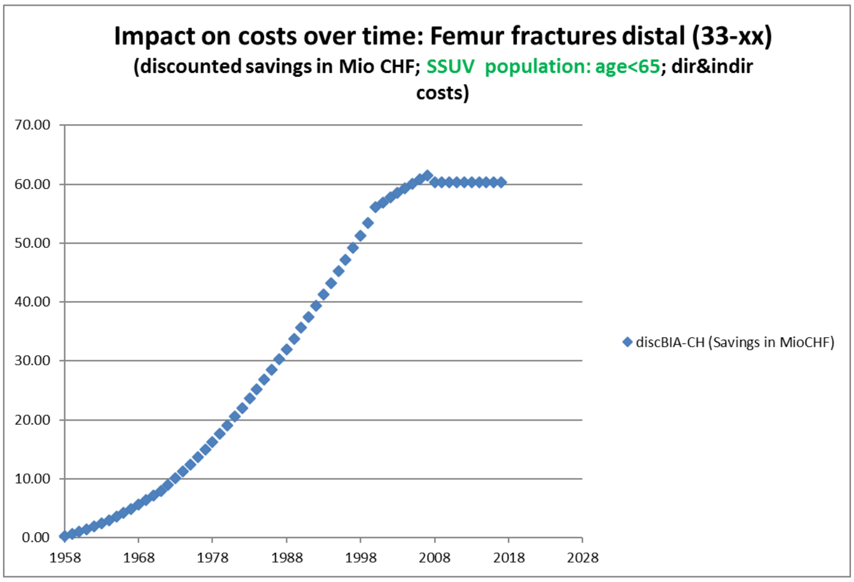

Figure 3.2: **Annual savings in total costs (OS vs. CONS) in patients with proximal femur fractures in Switzerland.** Each data point represents the savings of one specific calendar year in million 2015 Swiss Francs (CHF); discount rate 3%

For the period 1958 to 2017, extrapolation of savings in total costs for femur fracture treatment (all locations) to the modelled Swiss population (age <65) resulted in CHF 5.05 billion (in 2015 Swiss Francs; discount rate 3%).

The result of the extrapolation from Switzerland to all 17 high income countries (top down approach) is shown in Figure 3.3 (see also Table 3.5). For the period 1958 to 2017, total savings for femur fracture treatment (all anatomic locations) to the modelled population (age <65) resulted in CHF 239 billion (in 2015 Swiss Francs; discount rate 3%).

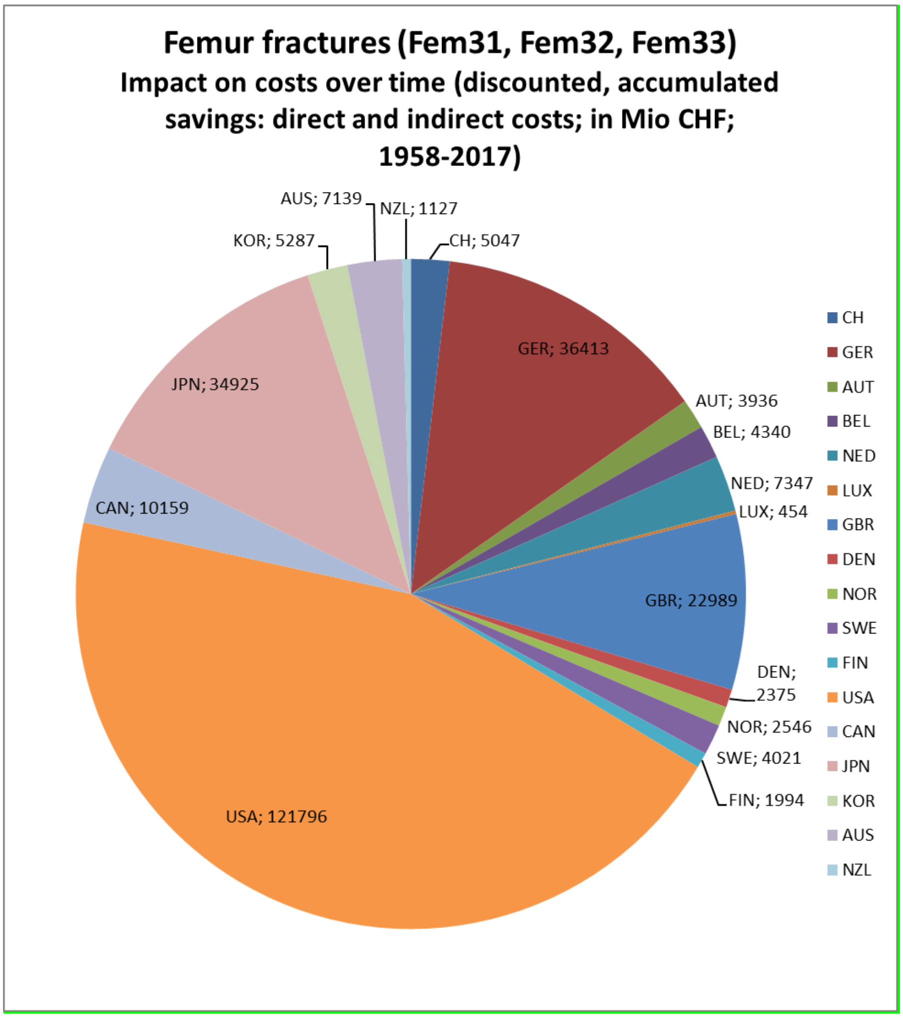

Figure 3.3: **Extrapolated savings in total costs (OS vs. CONS) in patients with femur fractures (all anatomic locations) in 17 high income countries 1958 to 2017.** In million 2015 Swiss Francs (CHF); discount rate 3%.

country	cost savings	(Dir&Indir)
CH	5047	
GER	36413	
AUT	3936	
BEL	4340	
NED	7347	
LUX	454	
GBR	22989	
DEN	2375	
NOR	2546	
SWE	4021	
FIN	1994	
USA	121796	
CAN	10159	
JPN	34925	
KOR	5287	
AUS	7139	
NZL	1127	
SUM	**271896**	Mio CHF

Table 3.5: **Extrapolated savings in total costs (OS vs. CONS) in patients with femur fractures (all anatomic locations) in 17 high income countries 1958 to 2017**. In million 2015 Swiss Francs (CHF); discount rate 3%. Dir&Indir: direct and indirect costs.

Results of the elderly population (age ≥70)

For elderly patients, we modelled only the impact of OS on proximal femur fractures, as this fracture type represent about 85% of femur fractures in this age group.[14] We estimated only differences in direct medical costs. No indirect costs were calculated in this age group beyond working age. We used the same cost input variables as for the working population, but applied an age-specific caseload per year and age specific complication rates.[1,15,16]

The overall picture is similar to the one found for the working population. Annual savings in total costs for treatment of proximal femur fractures in the elderly population increased from 1958 to 2017, mainly due to an increasing technology penetration rate and a changing epidemiology of fractures (Figure 3.4).

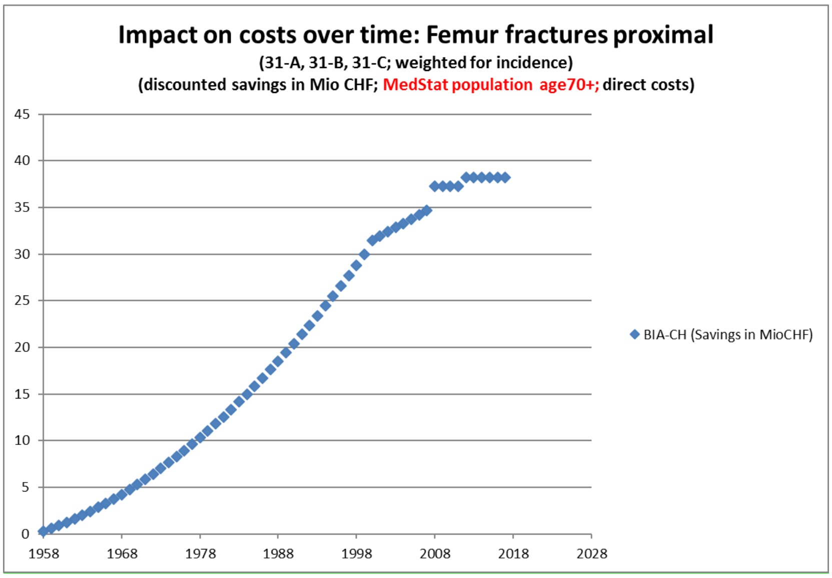

Figure 3.4: **Annual savings in total costs (OS vs. CONS) in patients with proximal femur fractures in Switzerland.** Each data point represents the savings of one specific calendar year in 2015 million Swiss Francs (CHF); discount rate 3%

For the period 1958 to 2017, total savings in direct medical costs for treatment of proximal femur fractures in the modelled Swiss elderly population (age ≥70) resulted in CHF 1.1 billion (in 2015 Swiss francs; Table 3.6). The extrapolation to all 17 high income countries resulted in CHF 69 billion (in 2015 Swiss francs). Our modelled incidence of low-impact hip fractures was 154 cases/100'000 inhabitants per year, which was derived from the Swiss hospital statistics.[14] This incidence was in the range of published data from several other high income countries. [17-20]

country	cost savings (Direct costs)	
CH	1157	
GER	8556	
AUT	925	
BEL	1064	
NED	1777	
LUX	111	
GBR	5559	
DEN	574	
NOR	616	
SWE	973	
FIN	482	
USA	31938	
CAN	2663	
JPN	9153	
KOR	1570	
AUS	1871	
NZL	295	
SUM	**69285**	Mio CHF

Table 3.6: **Extrapolated total savings (OS vs. CONS: direct medical costs) in elderly patients (age ≥70) with proximal femur fractures in 17 high income countries 1958 to 2017**. In million 2015 Swiss Francs (CHF).

We modelled life years gained by OS compared to CONS using higher mortality rates for this particular age group (1 year mortality after proximal femur fracture: OS: 20%; CONS: 60%). Again, we applied the age-specific caseload per year.

Life years gained per year in the elderly population with proximal femur fractures increased from 1958 to 2017, depending on technology penetration and epidemiology of fractures (Figure 3.5).

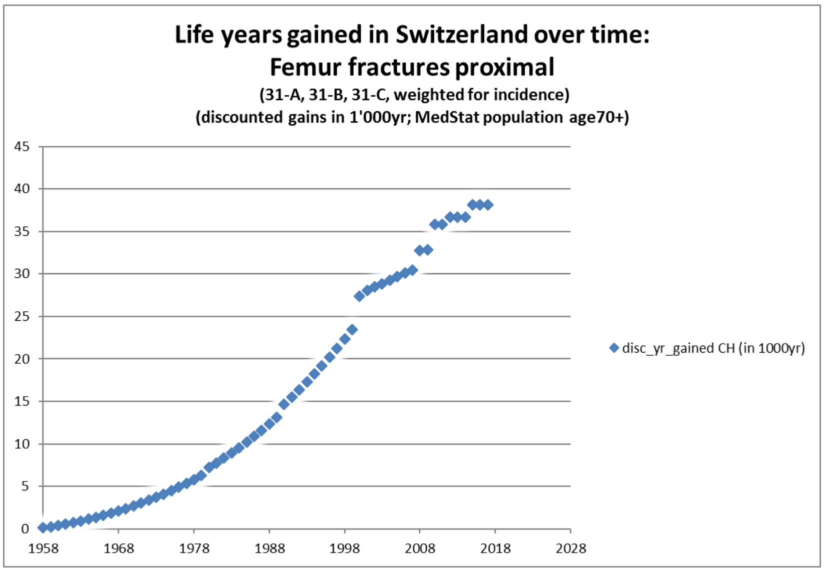

Figure 3.5: **Annual number of life years gained (OS vs. CONS) in patients with proximal femur fractures in Switzerland.** Each data point represents the life years gained (in 1000yr) of one specific calendar year; discount rate 3%.

For the period 1958 to 2017, extrapolation of the number of life years gained for treatment of proximal femur fractures in the modelled Swiss elderly population (age ≥70) resulted in 0.9 million life years gained (Table 3.7). The extrapolation to all 17 high income countries resulted in 73 million life years gained.

country	disc_yr_gained (in 1000yr)	
CH	940	
GER	8924	
AUT	938	
BEL	1181	
NED	1806	
LUX	58	
GBR	6752	
DEN	595	
NOR	544	
SWE	1034	
FIN	581	
USA	28769	
CAN	3304	
JPN	12361	
KOR	2637	
AUS	2187	
NZL	417	
SUM	**73030**	(in 1000yr)

Table 3.7: **Extrapolated number of life years gained (OS vs. CONS) in elderly patients (age ≥70) with proximal femur fractures in 17 high income countries 1958 to 2017.** In 1000 years; discount rate 3%.

3.2.2 Tibia fractures

Key findings for the population age <65:

- Savings due to OS compared to CONS in patients with tibia fractures (age <65) are CHF 104’000 per patient (direct and indirect costs) which is mainly due to savings of indirect costs (CHF 102’000).
- For the period 1958 to 2017, extrapolation of these savings to the modelled Swiss population with tibia fractures (age <65) resulted in CHF 9.8 billion.
- For the period 1958 to 2017, extrapolation of total savings for tibia fracture treatment in 17 high income countries (age <65) resulted in CHF 507 billion.
- The extrapolation to all 17 high income countries resulted in 2.1 million life years gained (about 2/3 of these life years gained before age 65 and included in productivity gains, i.e. indirect cost savings)

Included population

Baseline data of our modelled population for tibia fractures in Switzerland are depicted in Table 3.8 (working age population; age <65).

	Tibia proximal	Tibia shaft	Tibia distal	total
n (2011)	2042	405	731	3178
n (total 1958 to 2017)	65180	119612	26182	210974
age (mean) at injury	41.7	39.9	41.5	
sex ratio (female)	0.43	0.22	0.24	
time span to age 65	22.87	24.88	23.26	
modelled person years	1490667	2975947	608996	5075609

Table 3.8: **Baseline data of working age population with femur fractures (SSUV population; age <65 years) as used for the estimation of direct and indirect costs.**

In the working age population, we estimated 210’974 tibia fracture cases (all locations) from 1958 to 2017 with over 5 Mio modelled person years.

Results of working age population (age <65)

In patients with tibia fractures, direct medical costs in Switzerland are lower for OS (CHF 17’088) compared to CONS treatment (CHF 18’954). While the acute care (hospital) costs for OS are higher compared to CONS treatment, a longer rehabilitation period for patients with conservative treatment finally leads to higher direct medical costs in this group in our decision tree model (Table 3.9).

Indirect costs in Switzerland are substantially lower for OS (CHF24’934) compared to CONS treatment (CHF 128’831) in this patient group. With OS, patients have a shorter period of absence from work compared to CONS and higher return to work rates. In addition, lower mortality rates (OS: 0.1%; CONS: 1%) lead to decreased productivity losses due to premature death before age 65.

In summary, savings due to OS compared to CONS in patients with tibia fractures in this age group are CHF 105’000 per patient, which is mainly due to savings of indirect costs (CHF 103’000).

anatomic localisation of fracture	YEAR	AO/OTA	treatment	exp cost direct	exp cost indirect	exp cost total
Tibia prox	2015	41-xx	OP	12868	19926	32'794
	2015		CONS	18942	122690	141'632
Tibia dia (shaft)	2015	42-xx	OP	20775	28487	49'262
	2015		CONS	18942	129117	148'059
Tibia dist	2015	43-xx	OP	26115	36154	62'269
	2015		CONS	18992	145105	164'097
Tibia total costs (CHF weighted average; per patient)		41-43	OP	17088	24934	42023
			CONS	18954	128831	147785
Difference in total costs Tibia (CHF per patient: CONS-OP)		41-43		**1865**	**103897**	**105762**

Table 3.9: **Expected direct and indirect costs of tibia fractures (working age population; age <65) in Switzerland.** Costs are in 2015 Swiss Francs (CHF). Tibia total costs are weighted for relative frequency of tibia fracture locations.

The co-occurrence of higher return-to work rates and lower direct and indirect costs, make OS a dominant intervention comparted to CONS in this patient group (Figure 3.6; example for tibia shaft fracture).

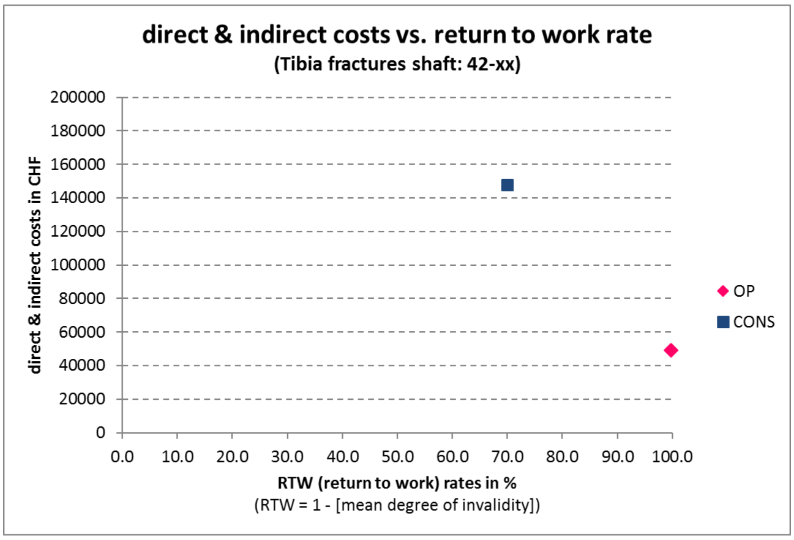

Figure 3.6: **Cost-effectiveness plot of OS vs. CONS in patients with tibia shaft fractures.** Patient benefit (return to work rate) is depicted against total costs (i.e. direct plus indirect costs). Costs are in 2015 Swiss Francs (CHF).

Annual savings in total costs for tibia fracture treatment increased from 1958 to 2017, depending on technology penetration and epidemiology of fractures (Figure 3.7; example for distal tibia fractures).

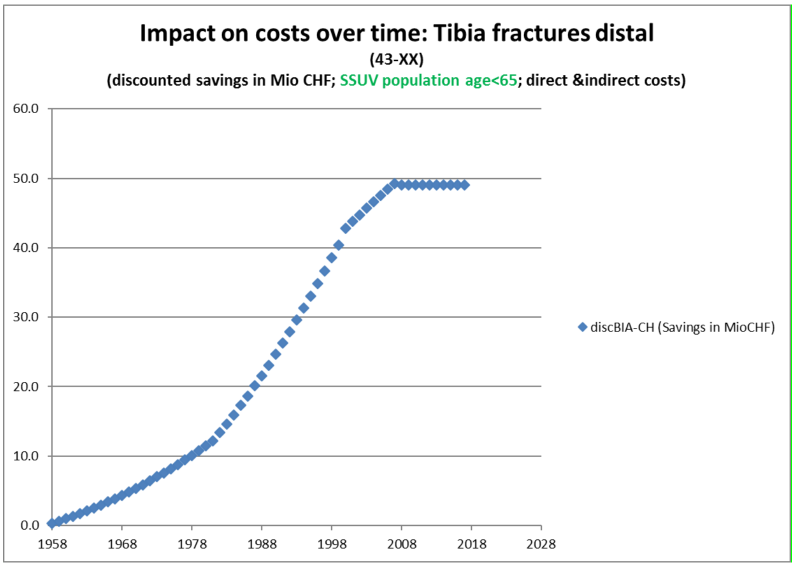

Figure 3.7: **Annual savings in total costs (OS vs. CONS) in patients with distal tibia fractures in Switzerland.** Each data point represents the savings of one specific calendar year. Costs (i.e. direct plus indirect costs) are in 2015 million Swiss Francs (CHF);discount rate 3%.

For the period 1958 to 2017, extrapolation of savings in total costs for tibia fracture treatment (all locations) to the modelled Swiss population (age <65) resulted in CHF 9.8 billion (in 2015 CHF; discount rate 3%).

The extrapolation of the results from Switzerland to additional16 high income countries worldwide (top down approach) is shown in Figure 3.8 (see also Table 3.10).

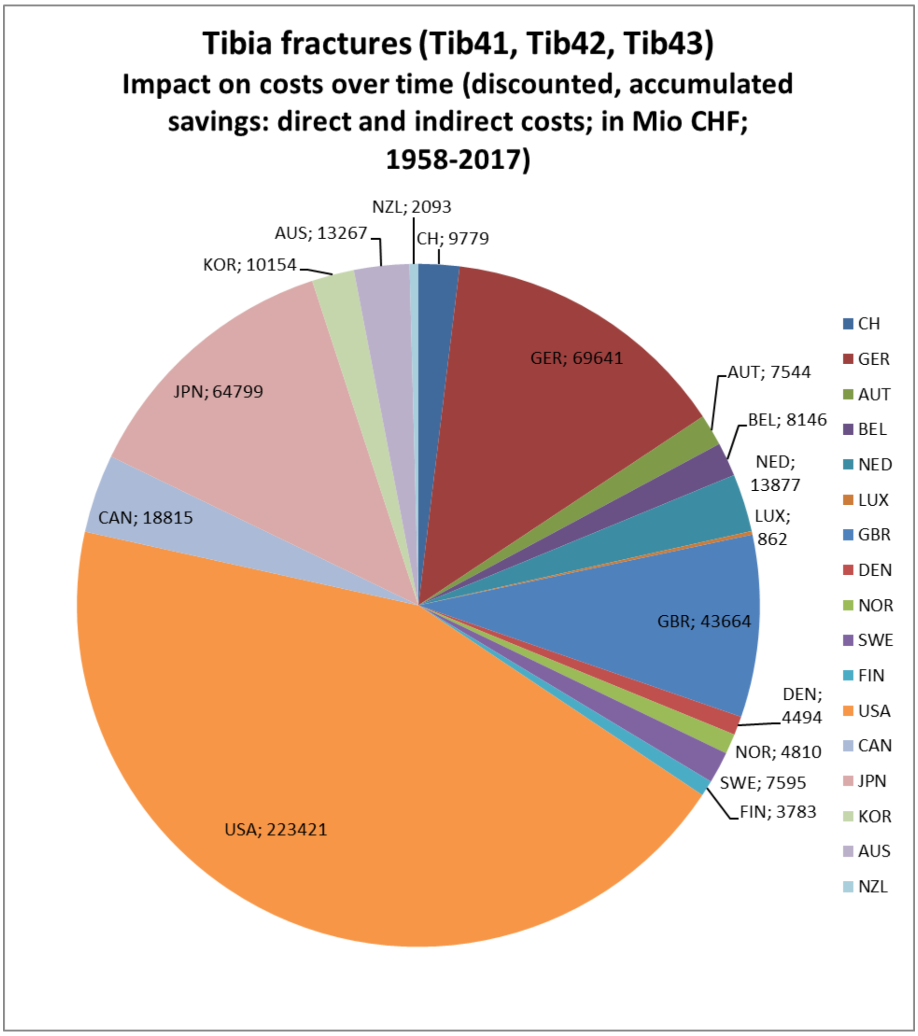

Figure 3.8: **Extrapolated savings in total costs (OS vs. CONS) in patients with tibia fractures (all anatomic locations) in 17 high income countries 1958 to 2017.** In million 2015 Swiss Francs (CHF); discount rate 3%.

For the period 1958 to 2017, extrapolation of savings in total costs for femur fracture treatment (all anatomic locations) to the modelled population (age <65) of 17 high income countries resulted in CHF 506 billion (in 2015 CHF; discount rate 3%; Table 3.10).

country	BIA (savings D&I)	
CH	9779	
GER	69641	
AUT	7544	
BEL	8146	
NED	13877	
LUX	862	
GBR	43664	
DEN	4494	
NOR	4810	
SWE	7595	
FIN	3783	
USA	223421	
CAN	18815	
JPN	64799	
KOR	10154	
AUS	13267	
NZL	2093	
SUM	**506744**	Mio CHF

Table 3.10: **Extrapolated savings in total costs (OS vs. CONS) in patients with tibia fractures (all anatomic locations) in 17 high income countries 1958 to 2017**. In million 2015 Swiss Francs (CHF); discount rate 3%. Dir&Indir: direct and indirect costs.

3.2.3 Radius fractures

Key findings for the population age <65:

- Savings due to OS compared to CONS in patients with radius fractures (age <65) are CHF 13’700 per patient (higher direct costs: CHF +4’500; lower indirect costs: CHF -18’200).
- For the period 1958 to 2017, extrapolation of these savings to the modelled Swiss population with radius fractures (age <65) resulted in CHF 1.5 billion.
- For the period 1958 to 2017, extrapolation of total savings for radius fracture treatment in 17 high income countries (age <65) resulted in CHF 77 billion.

Included population

Baseline data of our modelled population for radius fractures in Switzerland are depicted in Table 3.11 (working age population; age <65).

	Radius proximal	Radius shaft	Radius distal	total
n (2011)	905	119	4429	5453
n (total 1958 to 2017)	47998	17054	247010	312062
age (mean) at injury	39.7	39.3	42.7	
sex ratio (female)	0.44	0.35	0.52	
time span to age 65	24.86	25.35	21.78	
modelled person years	1193218	432325	5379878	7005421

Table 3.11: **Baseline data of working age population with femur fractures (SSUV population; age <65 years) as used for the estimation of direct and indirect costs.**

We included for radius fractures in our model only the rate of fracture cases, where an indication for OS is given according to current practice for each fracture location (age <65 years: radius proximal: 65%; radius shaft: 100%; radius distal: 90%).[21,22] Only in this subgroup of radius fractures, OS can have an impact on patient care with respect to patient benefit or costs. This is in contrast to femur and tibia fractures, where the number of patients with a fracture diagnosis is today almost identical with the number of patients with clear indication for OS.

In the working age population, we finally estimated 312'000 radius fracture cases with indication for OS (all locations) from 1958 to 2017 with 7 Mio modelled person years.

Results of working age population (age <65)

In patients with radius fractures, direct medical costs in Switzerland are higher for OS (CHF 10'294) compared to CONS treatment (CHF 5'810; Table 3.12). While the acute care (hospital) costs for OS are higher compared to CONS treatment, no substantial post-acute cost difference between the two treatment strategies are assumed in our decision tree model).

Indirect costs in Switzerland are lower for OS (CHF 10'643) compared to CONS treatment (CHF 28'853) in this patient group due to shorter absence from work and lower degrees of invalidity with OS. Productivity losses due to premature death before age 65 are not a relevant issue for radius fractures and we assumed mortality rates of 0% for both strategies.

In summary, savings due to OS compared to CONS in patients with radius fractures in this age group are CHF 13'700 per patient. Higher direct medical costs of OS (CHF +4500) are overcompensated by savings in indirect costs (CHF -18'200).

anatomic localisation of fracture	YEAR	AO/OTA	treatment	exp cost direct	exp cost indirect	exp cost total
Radius prox	2015	21-xx	OP	10808	9866	20'674
	2015		CONS	5810	26557	32'367
Radius shaft	2015	22-xx	OP	9442	11583	21'025
	2015		CONS	5810	42858	48'668
Radius dist	2015	23-xx	OP	9442	12143	21'585
	2015		CONS	5810	26346	32'156
Radius total costs (CHF weighted average; per patient)		21-23	OP	10294	10643	20937
			CONS	5810	28853	34663
Difference in total costs Radius (CHF per patient: CONS-OP)		21-23		**-4484**	**18210**	**13726**

Table 3.12: **Expected direct and indirect costs of radius fractures (working age population; age <65) in Switzerland.** Costs are in 2015 Swiss Francs (CHF). Radius total costs are weighted for relative frequency of radius fracture locations.

Modelled return-to work rates and (combined) direct and indirect costs for OS and CONS in this patient group are depicted in Figure 3.9 (example for distal radius fractures).

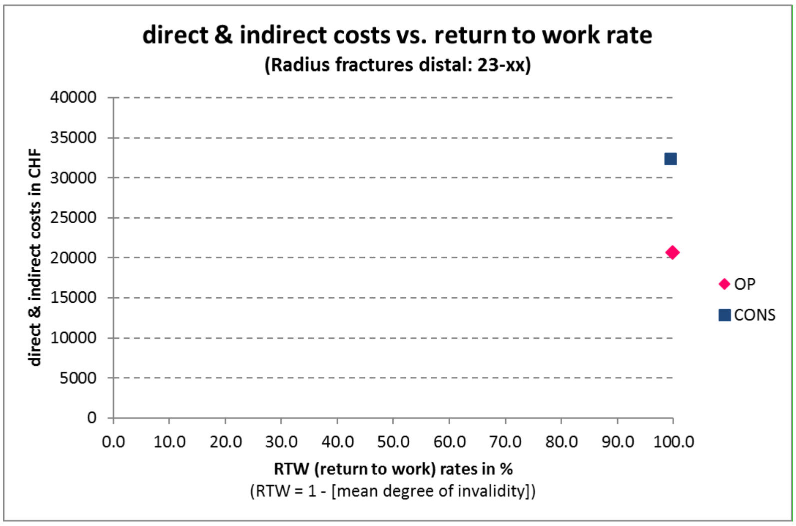

Figure 3.9: **Cost-effectiveness plot of OS vs. CONS in patients with radius shaft fractures.** Patient benefit (return to work rate) is depicted against total costs (i.e. direct plus indirect costs). Costs are in 2015 Swiss Francs (CHF).

Annual savings in total costs for radius fracture treatment increased from 1958 to 2017, depending on technology penetration and epidemiology of fractures (Figure 3.10; example for distal radius fractures).

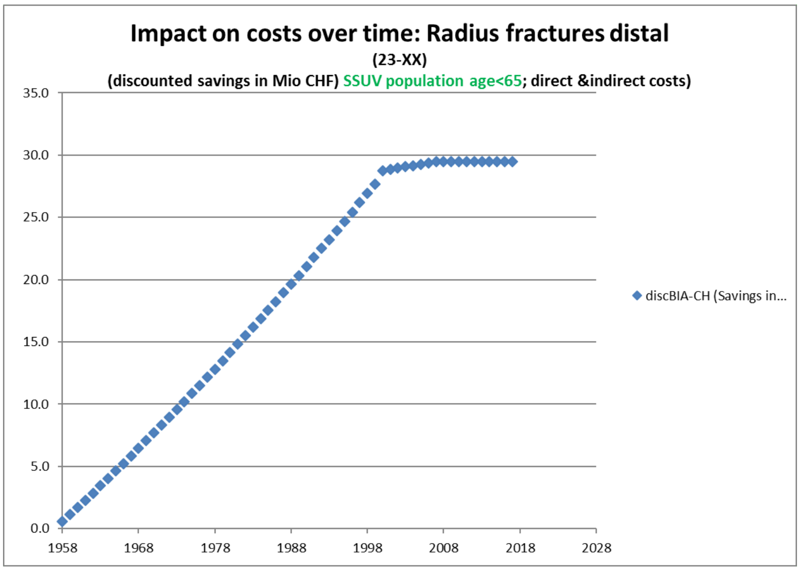

Figure 3.10: **Annual savings in total costs (OS vs. CONS) in patients with distal radius fractures in Switzerland.** Each data point represents the savings of one specific calendar year. Costs (i.e. direct plus indirect costs) are in 2015 million Swiss Francs (CHF);discount rate 3%.

For the period 1958 to 2017, extrapolation of savings in total costs for radius fracture treatment (all locations) to the modelled Swiss population (age <65) resulted in CHF 1.5 billion (in 2015 CHF; discount rate 3%).

The extrapolation of the results from Switzerland to additional16 high income countries worldwide (top down approach) is shown in Figure 3.11 (see also Table 3.13).

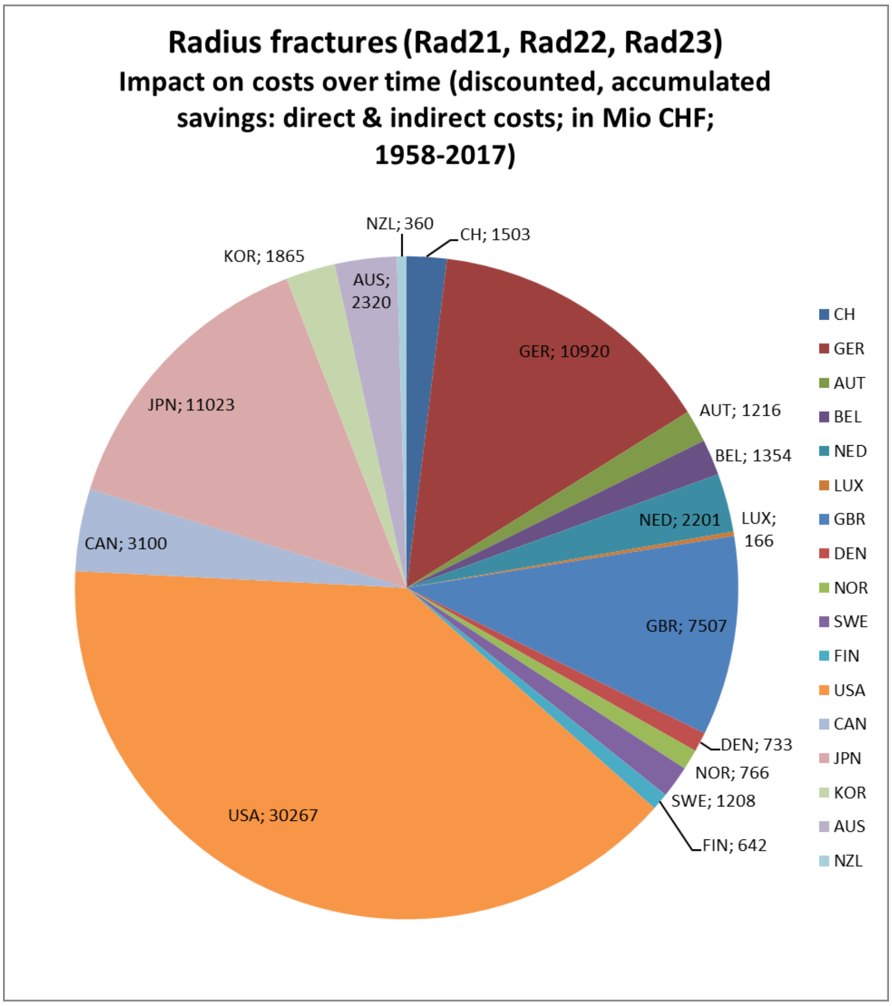

Figure 3.11: **Extrapolated savings in total costs (OS vs. CONS) in patients with radius fractures (all anatomic locations) in 17 high income countries 1958 to 2017.** In million 2015 Swiss Francs (CHF); discount rate 3%.

For the period 1958 to 2017, extrapolation of savings in total costs for femur fracture treatment (all anatomic locations) to the modelled population (age <65) of 17 high income countries resulted in CHF 77 billion (in 2015 CHF; discount rate 3%; Table 3.13).

country	BIA (savings D&I)	
CH	1503	
GER	10920	
AUT	1216	
BEL	1354	
NED	2201	
LUX	166	
GBR	7507	
DEN	733	
NOR	766	
SWE	1208	
FIN	642	
USA	30267	
CAN	3100	
JPN	11023	
KOR	1865	
AUS	2320	
NZL	360	
SUM	**77153**	Mio CHF

Table 3.13: **Extrapolated savings in total costs (OS vs. CONS) in patients with radius fractures (all anatomic locations) in 17 high income countries 1958 to 2017**. In million 2015 Swiss Francs (CHF); discount rate 3%. Dir&Indir: direct and indirect costs.

3.2.4 Sensitivity analyses

Results of our sensitivity analyses are shown in Table 3.14. A change of the discount rate has a sizeable effect on savings in direct and indirect costs for the three index bones (base case discount rate 3%: savings of CHF 856 bn; scenario 0%: CHF 1214 bn; scenario 6%: CHF 635 bn). For the elderly population, the range of life years gained (base case: 73 million) is between 85 million (discount rate 0%) and 63 million (discount rate 6%)

Assumed invalidity rates after complications with CONS have a leverage effect on indirect costs and, thus, on total costs (high degree of invalidity [base case scenario]: savings of CHF 856 bn; scenario intermediate invalidity: CHF 728 bn; scenario low invalidity: CHF 602 bn).

	Diff. D&I costs (savings: million CHF)	**Diff. D&I costs (savings: million CHF)**	**Diff. D&I costs (savings: million CHF)**	**Diff. D&I costs (savings: million CHF)**	**years of life gained** (until end of life expectancy; **(YLG: 1'000 years)**	**Diff. Direct costs (Savings: million CHF)**	**years of life gained** (until end of life expectancy; **(YLG: 1'000 years)**
population	working pop	working pop	working pop	working pop	working pop	elderly pop	elderly pop
included countries	17 high income	17 high income	17 high income	17 high income	17 high income	17 high income	17 high income
Sensitivity analysis	**Femur** AO/OTA 31-33	**Tibia** AO/OTA 41-43	**Radius** AO/OTA 21-23	**Sum of 3 index bones**	**Sum of 3 index bones**	**Femur prox** AO/OTA 31	**Femur prox** AO/OTA 31
Discount rate							
Base case (discount rate 3%)	**271'896**	**506'744**	**77'153**	**855'792**	**4'625**	**69'285**	**73'030**
discount rate 0%	385'143	705'225	123'190	1'213'558	8'238	n.a.	85'182
discount rate 6%	205'301	381'407	47'965	634'673	2'977	n.a.	63'304
CONS: Invalidity rate after complication							
Base case (BC)	BC: 100% invalidity	BC: 100% invalidity	BC: 20% invalidity				
Base case	**271'896**	**506'744**	**77'153**	**855'792**	n.a	n.a.	n.a.
CONS: invalidity after CX: 80% (femur/tibia)	244'183	435'874		728'357	n.a.	n.a.	n.a.
CONS: invalidity after CX: 60% (femur/tibia)	216'472	365'010		601'566	n.a.	n.a.	n.a.
CONS: invalidity after CX: 15% (radius)			48'300				
CONS: invalidity after CX: 10% (radius)			20'084				
International wages compared to CH (indicator: GDP per person ratio)							
Base case (GDP per person ratio)	**271'896**	**506'744**	**77'153**	**855'792**	n.a.	**69'285**	n.a.
10% lower wages internationally (GDP pp ratio x 0.9)	246'251	457'848	66'507	770'606	n.a.	62'747	n.a.
20% lower wages internationally (GDP pp ratio x 0.8)	220'607	408'952	55'861	685'420	n.a.	56'210	n.a.
most conservative case: (discount rate: 6%; CONS invalidity after CX: 60% femur/tiba & 10% radius; 20% lower int. wages)	133'722	222'764	4'002	360'488	n.a.	56'417	n.a.

Table 3.14: **Summary of sensitivity analyses.** Sensitivity analyses are shown for differences in direct and indirect costs and life years gained (femur, tibia and radius fractures of working age population; age <65), and for differences in direct costs and life years gained (proximal femur fractures of elderly population; age ≥70). All costs are 2015 Swiss Francs (CHF). CONS: conservative therapy of fracture; CONS: conservative therapy; CX: complication mal-union or non-union after CONS.

We estimated savings of total costs due to OS of fractures of the three index bones over 60 years in the 17 selected high income countries of CHF 850 bn. (base case “best guess” at discount rate 3%; most conservative case in one-way sensitivity analyses: CHF 360 bn.; currency: 2015 Swiss Francs).

3.3 Impact on Spine, CMF and VET care

The principles of fracture management in trauma care have been leveraged within the AO in Spine, CMF (craniomaxillofacial) and VET (veterinary) care. For example, before the invention of OS, patients with complex CMF fractures were often treated with cerclage. Such an approach had serious side-effects concerning nutrition uptake, quality-of-life and morbidity. After introduction of osteosynthesis in CMF care quality of life of these patients was significantly improved during therapy.

We have not formally assessed the impact of the AO principles of fracture management in these areas. Thus, we have not compared OS with conservative treatment as for the three index bones. However, the contribution of the AO in these areas was assessed on a descriptive quantitative level, underpinned with qualitative contributions of key peers.

The impact of the AO innovation on VET care was assessed indirectly via the work packages business, education and science and results can be found there.We have not analysed any treatment data of veterinary care.

Our findings for spine and CMF care

The spine and CMF patients of the Swiss working age population are a mix of patients treated with OS and those treated conservatively. For example, data from spine registries[23] often only report about patients with degenerative spine disease, which is not in the focus of our report. In the absence of detailed figures for the ratio of patients treated with OS, the health economic impact of OS for the health care system can only be assumed.

Our findings in the domains “Impact on Business”, “Impact on Education” and “Impact on Science” provide some few data about sales rates of OS products, education of clinical methods and progress in science related to spine and CMF care. This can be seen as indirect evidence for the patient volume and the progress that has been made by these well-established treatment options. Based on those figures, a relevant impact of the AO innovations on patient care can be assumed also in the spine and CMF domain.

Current figures of case load and direct and indirect costs for the 2011 Swiss working age population (age <65) are depicted in table 3.15 (two example fractures from spine care) and table 3.16 (two example fractures from for CMF care) [24] Mean absence from work for the four example fractures is quite short in the era of osteosynthesis.

	fractures vertebrae cervicales	**fractures vertrebrae thoracales**
ICD-10	S12.XX	S22.0X
n (2011)	352	671
age (mean) at injury	41.6	42.9
sex ratio (female)	0.20	0.39
time span to age 65	23.4	22.1
direct medical costs (mean)	20487	10299
direct and indirect costs (mean)	71378	24653
absence from work (mth)	6.0	3.5
return to work rate (%)	98.3	99.6

Table 3.15: **Population descriptive data and costs in patients with spine fractures in Switzerland.** Costs are in 2011 Swiss Francs (CHF).

	fractures os zygomaticum and maxilla	**fractures mandibula**
ICD-10	S02.4X	S02.6X
n (2011)	473	342
age (mean) at injury	37.9	31.7
sex ratio (female)	0.21	0.25
time span to age 65 (years)	27.1	33.3
direct medical costs (mean)	9814	11252
direct and indirect costs (mean)	18479	15605
absence from work (mth)	2.0	1.6
return to work rate (%)	99.8	100

Table 3.16: **Population descriptive data and costs in patients with CMF fractures in Switzerland.** Costs are in 2011 Swiss Francs (CHF).

Conclusions:

Similar savings due to OS may have been realised per patient in spine and CMF care as for the three index bones, when an indication for OS is given. This may be especially the case for cervical spine trauma patients, where total costs are still high in the era of OS (mean direct and indirect costs per patient: CHF 71’000).

4 Impact on Education (WP2)

Without doubt, the AO's fame and reputation is heavily based on its "AO courses", its core educational activities. The engagement in training and education is an essential reason for the worldwide acceptance of osteosynthesis and for the long-term success of the AO. The AO courses played an essential role in the training of surgeons willing to use the "AO technique", i.e. high quality osteosynthesis based on sound, standardized and empirically validated methods and procedures. However, the AO courses' impact went way beyond the immediate effects of knowledge transfer. Of equal importance were the networks between fellow surgeons that were built and fostered during such activities. Finally, the commercial success of the Synthes products was largely due to the AO courses where participants got acquainted with Synthes materials and tools and were introduced to new products directly from their peers. While not intentionally conceived as such, the AO courses not only turned out to enhance the AO's prestige and credibility, but also to promote the sale of Synthes products [5].

4.1 Methodological approach of this work package

Direct as well as indirect effects of education are generally hard to capture. To cover the whole range of the AO's educational activities during the last 60 years we restrict the analysis to the input side: the amount of educational activities the AO conducted. Of course, by counting courses and participants, we can only grasp the essential impact the AO had on the worldwide diffusion of osteosynthesis. However, participation in an AO course is a good proxy of a surgeon's strong interest and likely future use of the AO technique – which makes course participation an important measure to look at. It is probably the best indicators of the diffusion of the AO technique and, at least in the early years, of modern osteosynthesis in general. Thanks to various sources, such as Schneider [25], Schlich [5] but especially to documents provided by Claudio Gubser[1], we are able to present a detailed

[1] We thank Claudio Gubser for kindly providing us access to the detailed course data.

picture not only of the number of courses and course participants of the “Davos courses”, but also of the AO courses held worldwide. From the course numbers we can derive a rough estimate of delivered teaching days. However, due to the changing nature of the courses over time and the different types of courses, these estimates must be interpreted with some reservation.

4.2 Results

Key findings:

- 65’000 surgeons were trained in the “Davos courses” 1960 to 2016
- 580’000 surgeons were trained in worldwide courses outside Switzerland 1965 to 2016
- 8’700 courses were held with about 20’000 teaching days delivered in worldwide courses 1965 to 2016
- 7’800 surgeons participated in fellowship programs 1971 to 2017

4.2.1 The “Davos Courses”

The “Davos Courses” were – and possibly still are – clearly the AO’s flagship educational activity. They soon became very popular among surgeons worldwide and were very international from the beginning: almost 90% of the participants from 1960 to 1982 were non-Swiss [5]. The first AO course in Davos took place in December 1960 with 66 participants. Subsequent courses had been organized every year with only one single interruption in 1962. The initial idea of the courses was to make fellow surgeons acquainted with the AO technique and with the corresponding Synthes materials and tools. This way, the AO principles and the standardized implementation of the “AO technique” should be promoted and the outcome of the AO technique improved. The “Davos Course” grew rapidly from a small gathering of friends, acquaintances and a few other interested peers into a large event. In 1969, the “Davos course” already had 530 participants and was hosted in the newly opened Davos conference center [5]. The number of course participants rose steadily and reached 2’000 in 2010. Since then, it remained at a high level fluctuating between

1'800 and 2'000 yearly participants (see figure 4.1). From 1960 to 2016, the total participants number sums up to approx. 65'000. This number overestimates the number of individual surgeons that came to Davos in order to get acquainted with the AO technique or to improve their osteosynthesis skills as many have participated in more than one course[2].

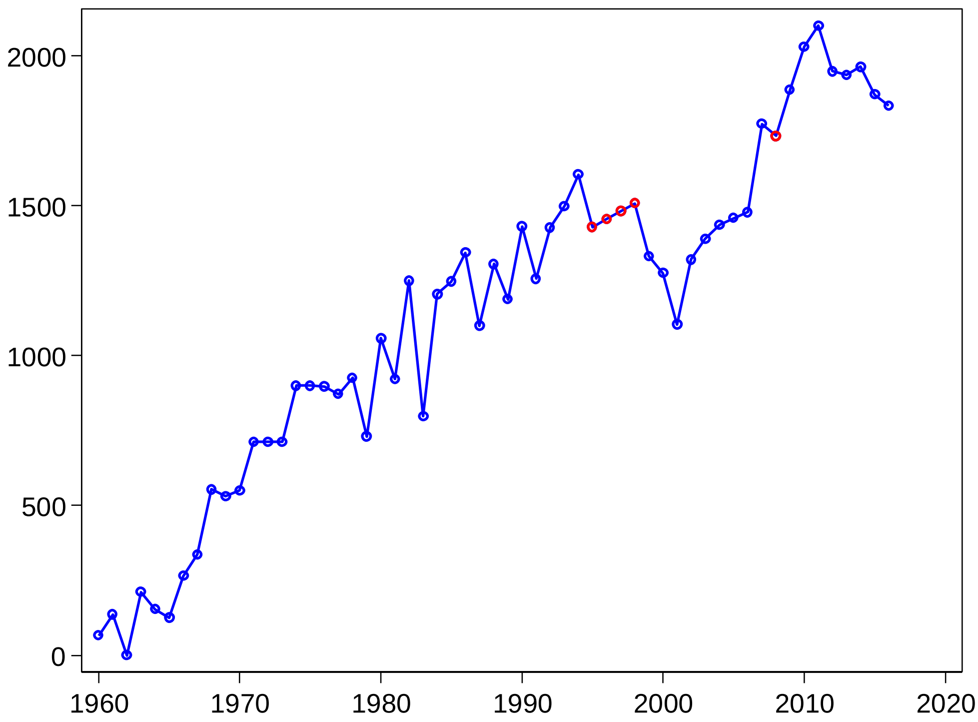

Figure 4.1: **AO "Davos Courses" participants 1960 to 2016**. Included are courses from all divisions, as well as "special courses" and "symposia". The years 1995-98 with missing data and 2008 with an unexplainable outlier were imputed using a polynomial regression function (red dots). Data source: Schneider [25], Schneider [26], Claudio Gubser, AO, HSG.

[2] We have data on "participations", i.e. participants that participated in more than one course are counted multiple times.

4.2.2 Worldwide AO Courses

Soon after having established the “Davos course” in Switzerland, the AO realized the need for courses in other countries and started to organize local AO courses throughout the world. Despite the “Davos courses” being the main educational activity, the worldwide courses played an important role in the diffusion of the AO technique and in fostering the worldwide AO network. Furthermore, local AO courses indicate a demand for the AO technique in a particular country and a strong interest from the part of the AO to get a foot on the ground in a particular place [5]. The AO started with a first local course in West Germany in 1965, held a course in Yugoslavia in 1968, in Canada in 1969, and in Austria and the US in 1970. Course numbers and places increased and by 1994, the AO already had held courses in 62 countries other than Switzerland. Figure 4.2 shows the introduction of AO courses by countries, i.e. the year a first AO course was organized in a country. Usually, courses were held on a regular basis after the first course took place. Clearly visible is the early development in Central Europe, North America, and Australia with courses starting in the sixties or early seventies. South America and the rest of the pacific region as well as India followed shortly afterwards in the late seventies/early eighties. The Near East, Russia and China had their first courses later in the late eighties or early nineties, shortly after the fall of the iron curtain. Sub-Saharan Africa, with the exception of South Africa, Nigeria, and Kenya, saw no AO courses before 1995.

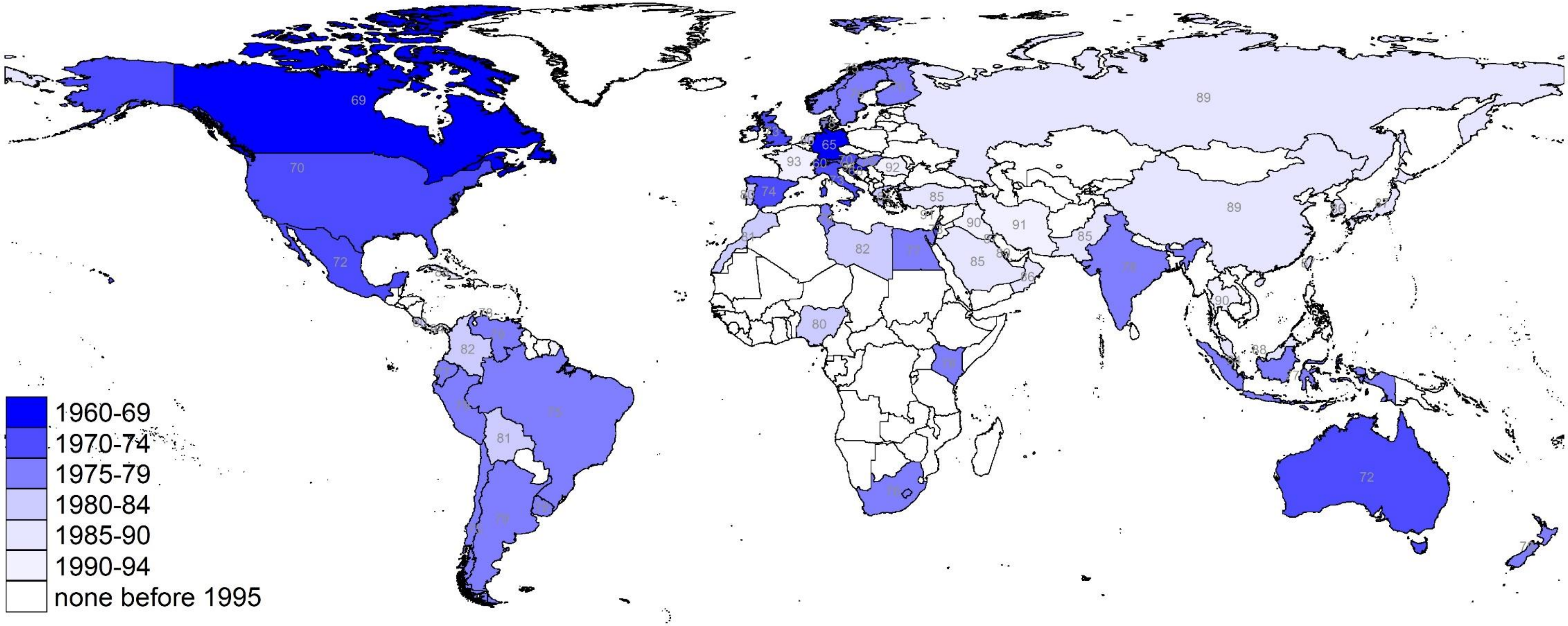

Figure 4.2: **Year of first AO course (up to 1994) by country**. Dark colors indicate an early introduction, light colors a late introduction. Data source: Schlich [5], Schneider [25]

The number of worldwide AO courses showed a steady increase from the late eighties on and increased sharply after the millennium when it surpassed 200 courses and 10’000 participants per year (see figure 4.3). In 2016, the AO held 727 courses for surgeons worldwide with 45’000 participants – excluding the Davos courses. Since their first local course outside Switzerland in 1965, the AO had held approx. 8’700 courses worldwide with 580’000 participants. Assuming an average course duration of 2.5 days, the AO has delivered about 20’000 teaching days. But what is perhaps more important, 580’000 surgeons in total, received an osteosynthesis training and improved their skills to the benefit of their patients in the whole world.

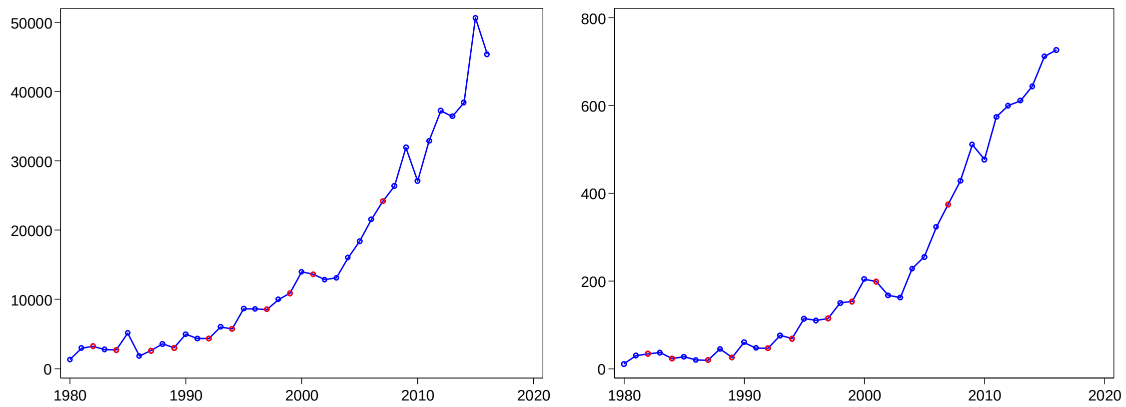

Figure 4.3: **Yearly AO course participants (left) and number of courses (right) 1980 to 2016 worldwide (excluding Davos courses).** Included are courses for surgeons from all divisions and also “special courses”, seminars, symposia, and, from 2008 onwards, webinars. Missing data (red dots) were imputed using a polynomial regression function. Data source: Claudio Gubser, AO, AO Community Development Managers.

The development of courses and the number of participants in particular countries give an interesting insight into the local standing of the AO and how it developed over time. Figure 4.5 depicts AO courses for some selected countries that had more or less regular AO courses taking place in the time period considered. Cleary, Germany and the US had most courses and developed at a similar pace with about 15 to 25 courses and between 1’500 and 2’000 participants per year after the turn of the millennium. The UK in contrast, in terms of market size comparable to Germany and the US, shows a much lower number of courses. It is beyond the scope of this study to detail the development in all of these countries. However, it is important to note, that they all have a slightly different story regarding the diffusion of osteosynthesis, the “AO technique” as well as the role the AO and the Synthes brand played in their markets.

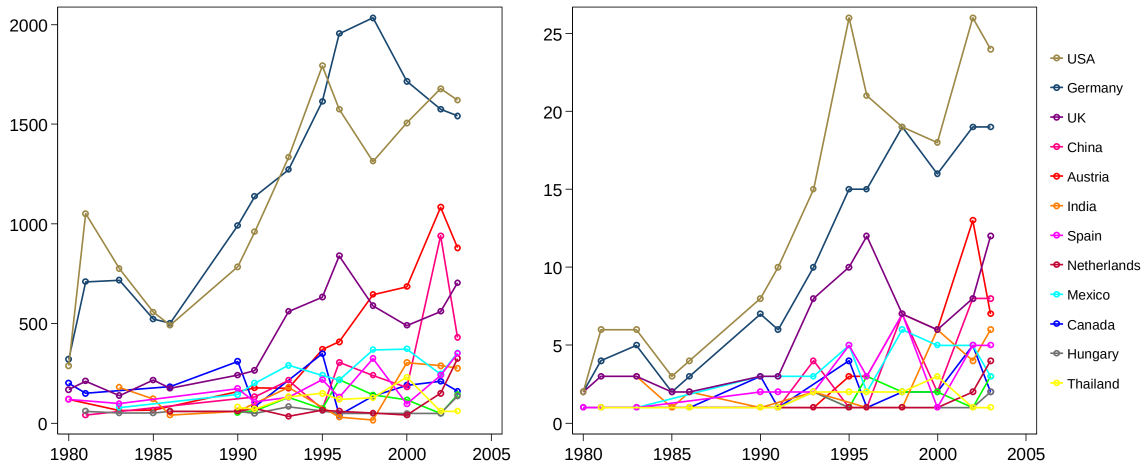

Figure 4.4: **Yearly AO course participants (left) and number of courses (right) 1980 to 2003 by selected countries**. No complete data for the whole time-series. Included are courses from all divisions and also “special courses”, seminars and symposia. Only countries with regular courses taking place during the considered period. Data source: Claudio Gubser, AO.

More recently, online materials such as videos, online courses, or webinars, and, in particular, the AO Surgery Reference, have become important resources for surgeons performing osteosynthesis and for fracture care in general. Reliable online sources that are accessible everywhere and anytime are very much appreciated by surgeons.[27] The AO Surgery Reference webpage that contains detailed instructions for the complete surgical management process for all fractures of any given anatomical region is a tool that is used by many surgeons worldwide. The reference webpage had about 40’000 returning visitors per month by early 2017. It is complemented by the AO Surgery Reference mobile app introduced in 2010, which has become widely used too. The app has been downloaded between 6’00 to 8’000 times per month since 2013 and was accessed by 140’000 users in one month by the beginning of 2017 (Data source: Urs Rüetschi, AO Education). These types of educational activities are certainly of essential importance and will play a leading role in the future – as did the classical courses in the past 60 years.

4.2.3 AO fellowships

Another important way of training surgeons and turning them into a sort of AO ambassadors in their home institutions and countries was the fellowship program that granted individual surgeons scholarships at AO hospitals, i.e. hospitals where AO members worked. In the beginning, these were only Swiss hospitals, later on also German and Austrian hospitals were included. Nowadays, there are about 130 active host hospitals all over the world.[3] The participants of the fellowship program were supposed to gain in-depth-knowledge and training in the use of the AO-technique. The program had 86 fellows in the first four years of its existence 1971 to 1974. It expanded rapidly to about 200 yearly participants from 1990 onwards. Then, from the mid-nineties to 2009 there was some stagnation. In 2015, finally, the number increased again remarkably to 296 participants (see figure 4.5). Note that for the years 2010 onwards, only trauma-fellowships are included due to lacking data on other division's fellowships. The seeming downward jump in 2010 is caused by this and does not reflect a decrease in overall fellowships. The overall fellowship number since 1971, when the program was initiated, amounts to approximately 7'800.

[3] In 2017: 22 in the Asia Pacific region, 63 in Europe, 5 in the Middle East, 30 in North America, and 9 in Latin America.

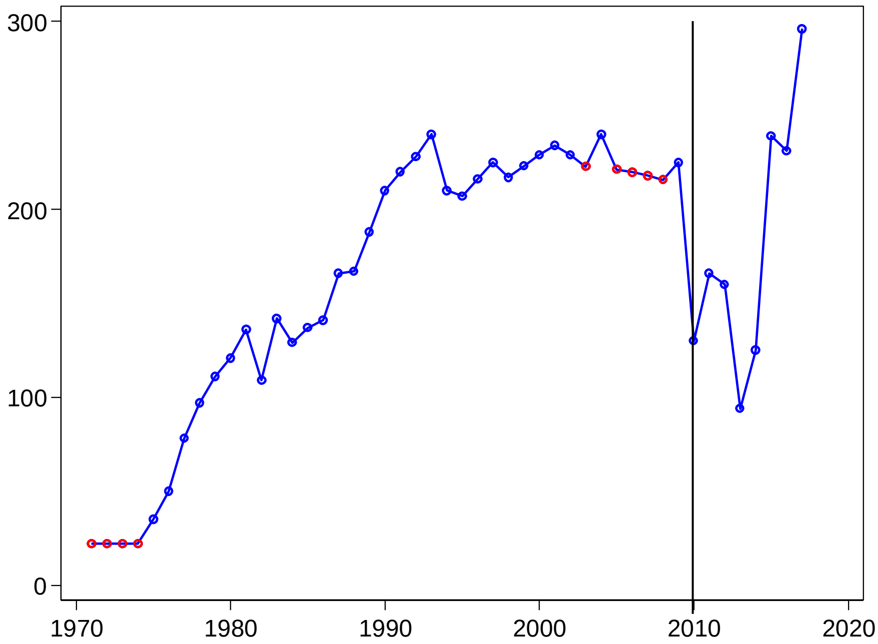

Figure 4.5: **Yearly AO fellowships 1971 to 2017**. For the years marked red only aggregate data (1971 to 1974) or no data (2003 to 2008) is available. Missing data was imputed using a polynomial regression function. For the years 2010 onwards, only trauma-fellowships are reported due to lacking data for other divisions. Data source: Schlich [2,] Schneider [23], AO Annual reports, AO Community Development Managers.

4.3 Impact on Education in Spine, CMF and VET care

More recently, the worldwide AO courses started to play an even more important role relative to the Davos courses and the yearly number of participants, including all divisions and operating room personal (ORP), increased in the last decade steadily from 33'000 in 2008 to 48'000 in 2016 (see figure 4.6). The number of courses delivered rose in the same period from 537 to 787. The majority of these courses were “trauma” courses, but the other divisions play an important role too and their relative importance is on the raise. For instance, the number of “spine” courses and participants increased not only in absolute numbers, but also relative to the trauma division: From 92 courses (with 3'913 participants) in 2008 to 180 courses (8'996 participants) in 2016. Hence, the number of spine courses and the corresponding participants doubled within eight years. The development of the CMF and the VET divisions show a similar absolute and relative increase, albeit with 112 courses (CMF) and 48 (VET) in 2016 at a lower level.

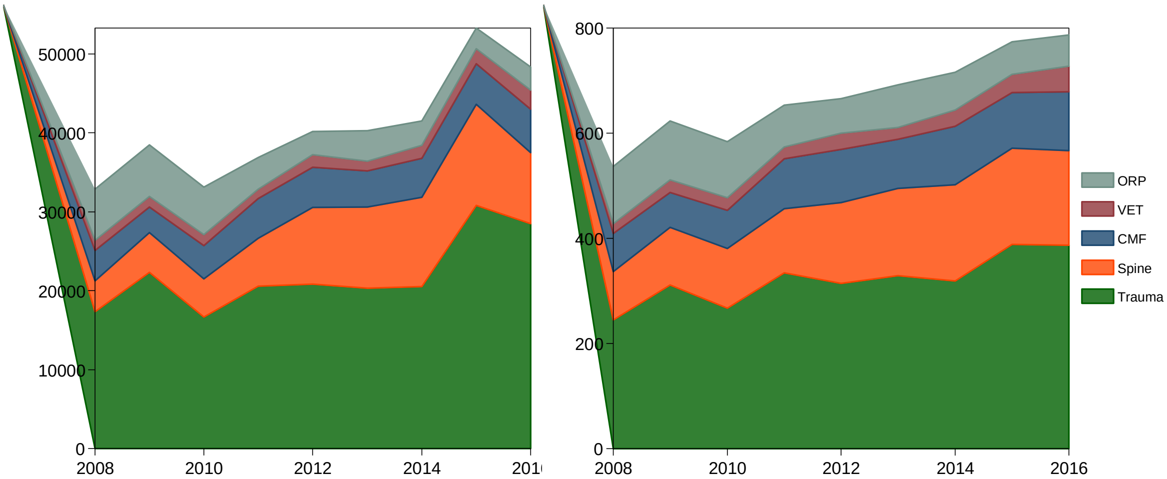

Figure 4.6: **Yearly AO course participants (left) and number of courses (right) 2008 to 2016 by divisions**. Included are courses for surgeons and operating room personnel (ORP), and also, “special courses”, seminars, symposia, and webinars. Data source: AO Community Development Managers.

5 Impact on Business of Medtech industry (WP3)

The AO was not only a highly successful professional education organization that played an essential role in the development and the successful establishment of osteosynthesis as a standard technique – it also supervised the production, marketing and sales of the osteosynthesis products it developed. Recognizing the need for appropriate materials, the AO got in contact with potential manufacturers right in its beginnings. Mathys, then a small instruments supplier for larger firms in the aviation sector, started 1958 to produce AO devices that were initially sold by the AO itself. Another producer, Straumann, joined 1960. In the same year, the AO formalized and professionalized its business activities by establishing the Synthes AG Chur, a non-profit company owned by the AO founders that received all actual and future intellectual property rights of the instruments and implants developed by the AO and its producers[5]. Mathys and Straumann received the exclusive production right for AO equipment, sold under the “Synthes” brand, in exchange for a royalty payment to the Synthes AG. The royalty payments were solely used to fund the AO’s research, documentation, and education activities. Synthes sales increased exponentially over time and not only provided to be a reliable and generous source for the funding of the

AO's activities – they generated a large international business on their own. From 1958 to 2017, overall Synthes sales, which comprise products sold by various producers under the Synthes brand, amounted to approximately CHF 55 Billion.

5.1 Methodological approach of this work package

Synthes product sales, the tools and materials developed by the AO and its producers for osteosynthesis, are – at least in the early years before competitors entered the markets – a good indicator of the diffusion of osteosynthesis and the frequency of its use. In addition, they show what a big economic impact an innovative idea in combination with a fruitful collaboration between surgery and industry could have. So far however, there have been no accounts of the actual business impact of the AO and its development over time in terms of actual sales of Synthes branded products. Partly, this is due to the special constellation between Synthes AG Chur as patent holder and the various producers. No complete sales data have been centrally collected. Overall sales figures from the individual producers, if procurable, cannot provide good information about Synthes sales, because most producers also sold other product lines. Mathys, for example, was involved in the development and production of hip replacements with Maurice Müller from 1963 onwards, which were then sold under the label Protek. Straumann started to produce dental implants in 1974. However, based on the royalty payments drawn from archival files of the Synthes AG Chur, we are able to provide historical time series of Synthes product sales since the very beginning of the AO for all producers and all countries.[4] These sales rates are at "royalty base prices", the prices that were mutually set by the producers and the AO when a new product was introduced. Final prices varied over time and between countries and were usually between 10 and 50% higher than the base prices.

5.2 Results

Key findings:

[4] We are indebted to Linus Heini, Curia Treuhand, for kindly providing us access and help in using the files as well as to Urs Jann and Peter Matter for pointing us to this valuable data source.

- Synthes sales of all producers at royalty base price 1961 to 2005 sum up to CHF 11,6 bn.
- Synthes US/Synthes Inc. sales at final prices from 1975 to 2016 sum up to CHF 54.5 bn.

5.2.1 Patent applications as a proxy for innovation

While the special partnership between surgeons and producers under the hood of the Synthes AG and the corresponding royalty payments effectively fueled AO's research and development of osteosynthesis, it also allowed the AO to retain control over the production, marketing, and sales process of its products. Testing of new products and the decision whether to introduce a new product into the market was decided by the AO, namely by its "Technische Kommission" (TK) which was established in 1961. An indicator of the innovative nature of this constellation is the number of patents that were submitted by the AO or, more precisely, by its formal patent holder, the Synthes AG Chur. In the beginning there were maximally one or two patent applications per year. It all started 1959 with a patent on a «Einrichtung zum chirurgischen Fixieren von Knochenfragmenten in Gliedmassen», a mechanism for the surgical fixation of bone fragments in extremities. Due to the growth of the AO and its innovative output (but also due to changing patent procedures and habits), the number of yearly patents increased slowly in the late seventies to about 5 per year (see figure 5.1). In the nineties about 20 patents per year were submitted and, since the turn of the millennium, between 35 and almost 60 per year and more. In 2006, Synthes AG Chur ceased to exist due to the sale of the AO patents and the Synthes brand to Synthes Inc. Hence, no more patents applications were made under its name.

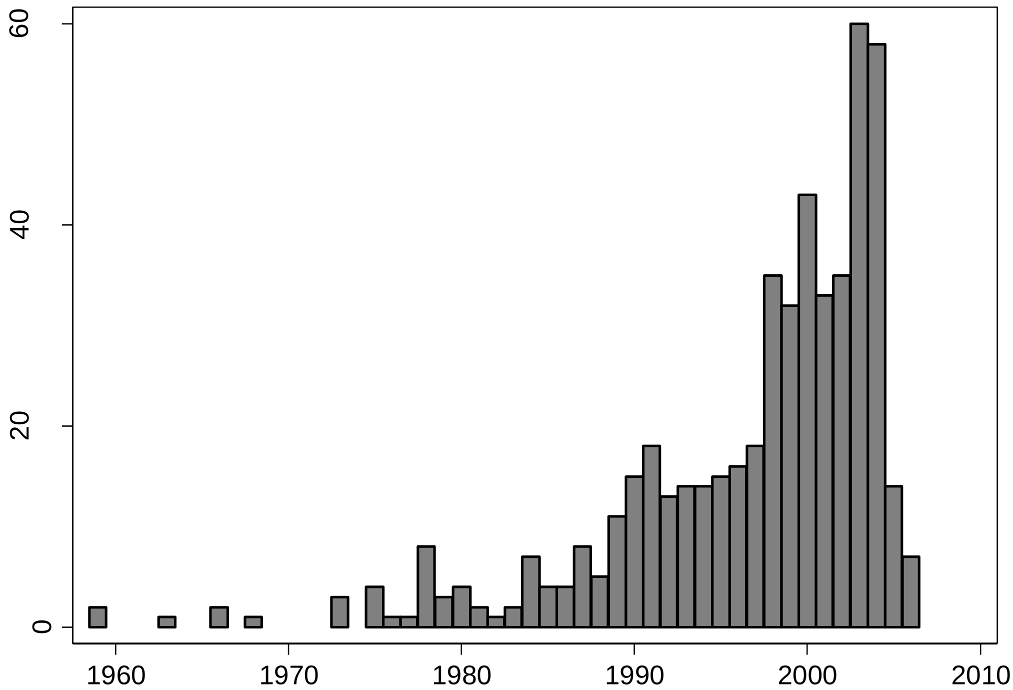

Figure 5.1: **Patent applications 1959-2006 of Synthes AG, Chur**. Data source: Christoph Nötzli, AO.

5.2.2 Synthes product sales

The special cooperation between producers and surgeons is seen by many as the key factor for both the establishment of the AO as a renowned professional group but also for the business success of the Synthes brand [5,28]. While the AO became highly influential and successful in the establishment of osteosynthesis as a standard technique in fracture care worldwide, the Synthes brand managed to establish itself as a trustworthy, reliable and innovative provider of osteosynthesis products. It paved the way for today's DePuy Synthes, which by 2016, was the leading osteosynthesis producer in Europe with a market share in trauma devices of almost 50%. Worldwide, Synthes' trauma division had a market share of 37% (Source: Depuy Synthes).

Figure 5.2 shows the early Synthes sales from 1961 to 1985 in "royalty base prices". Royalty base prices are the prices that were mutually set by the producers and the AO when a new product was introduced. Final prices varied over time and between countries and were usually between 10 and 50% higher than the base prices. In principle, end prices could also be lower than the base prices due to market developments, but this has rarely been the case. While we have no company specific data for the years 1961 to 1965, we see that the sales of Mathys and Straumann, the two original producers, developed similarly during the second half of the sixties. Then, however, Mathys was able to increase its sales faster than Strauman, the latter Stratec. Sales figures of the two companies started to diverge with Mathys having sales rates about one third higher than Straumann.

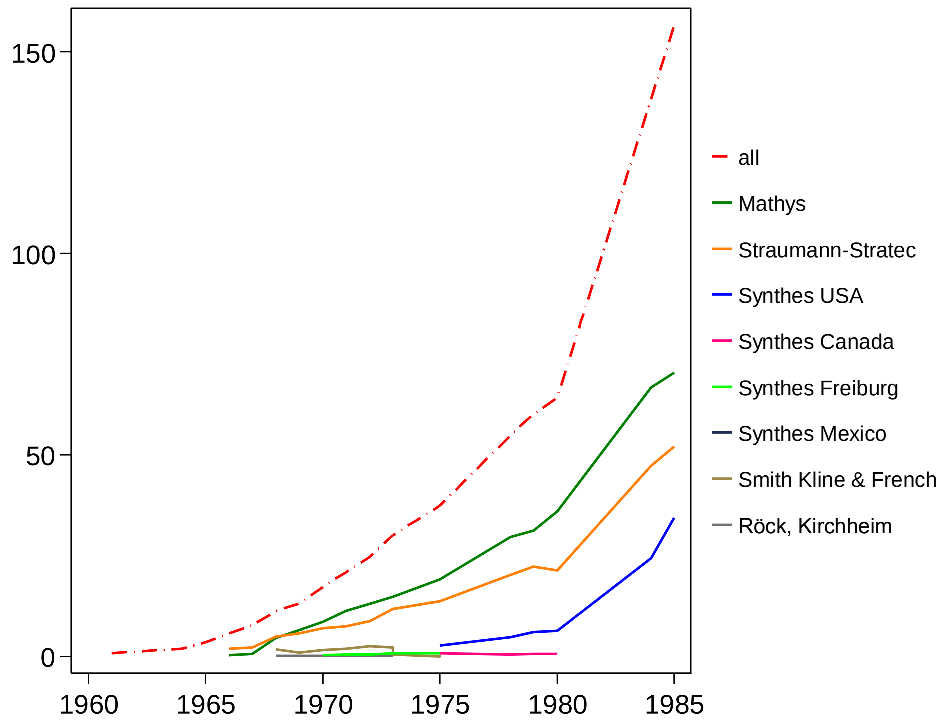

Figure 5.2: The early years: **Synthes products sales 1961-1985 by producer at royalty base prices (in Mio CHF)**. Years with missing data (74, 76, 77, 81, 82, 83, 86, 89, 90) imputed assuming linear increase from year to year. Data source: AO/Synthes annual finance reports.

In 1975, Synthes US, established in 1974, comes into the market and starts with sales at a very low level. Soon however, it manages to increase its sales considerably and catches up with both Straumann and Mathys (see figure 5.3). By 1997, Synthes US sold more than the other two producers together. Subsequently, the US market constantly showed much higher growth rates than the rest of the world. The US market, albeit with a substantial delay to other markets, provided to be a fertile ground for Synthes products.

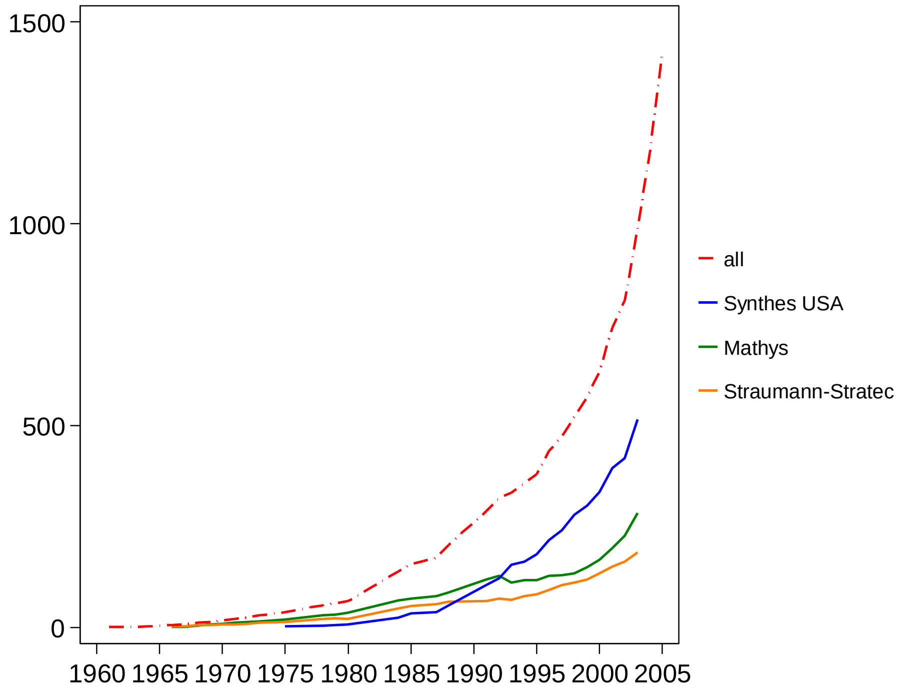

Figure 5.3: **Synthes products sales 1961-2005 by producer at royalty base prices (in Mio CHF)**. Years with missing data (74, 76, 77, 81, 82, 83, 86, 89, 90) imputed assuming linear increase from year to year. Data source: AO/Synthes annual finance reports.

For all producers together, there is an exponential increase in sales over time: with CHF 0.8 Mio in 1961, 3.5 Mio in 1965, 17 Mio in 1970, 64 Mio in 1980, 260 Mio in 1990, and 633 Mio in 2000. Overall Synthes sales, i.e. all the products sold under the Synthes brand owned by Synthes Chur AG from 1961 to 2005, sum up to a total of CHF 11'566 Mio (sales at base prices, end prices were about 10% to 50% higher).

Synthes US has turned into the largest Synthes producer since the early 90ies. After its mergers with Stratec in 1999 and Mathys in 2004, the resulting Synthes Inc. unified all formerly independent producers in one company and managed to increase sales even further. It passed 3'500 Mio annual sales in 2009 and kept that level up to the present (see figure 5.4). In 2011, Johnson & Johnson acquired Synthes. Overall, sales from Synthes US/Synthes Inc. from 1975 to 2016 sum up to a total of CHF 54'369 Mio (in final prices).

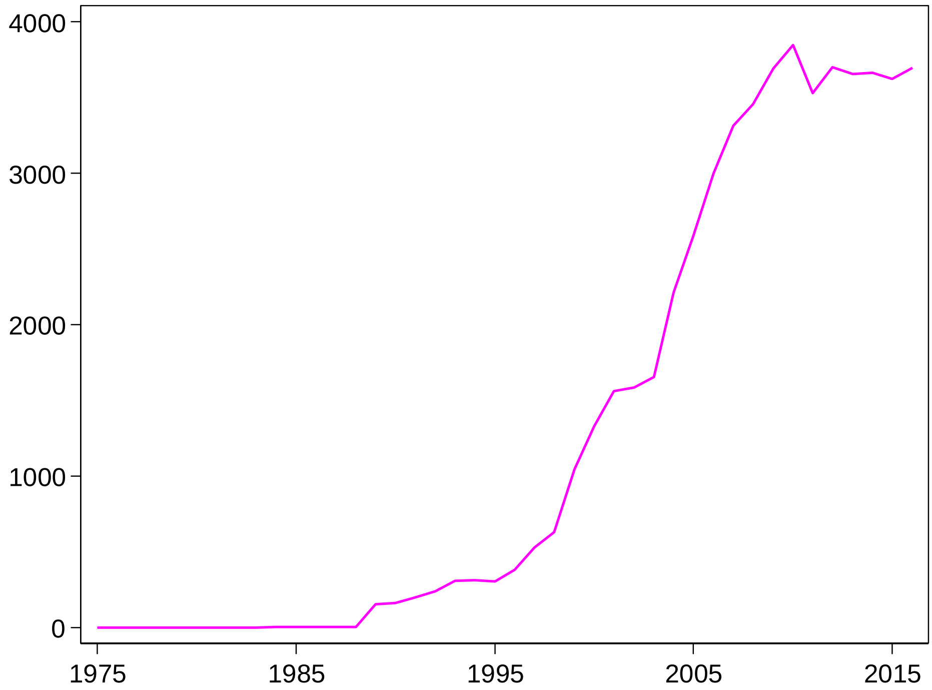

Figure 5.4: **Synthes US/Synthes Inc. products sales 1975-2016 (in Mio CHF)**. Data source: J&J DePuy Synthes.

The royalty data also allows detailed insights into the sales development in particular countries, which in the beginning corresponds pretty much to the diffusion of osteosynthesis in general. Figure 5.5 shows data for some selected countries with an early presence of AO and Synthes. While sales are increasing everywhere over time, the increase from the 1990ies onward, for instance, is much steeper for Germany (or the US, not shown in Figure 5.5) than for the UK and the other countries depicted.

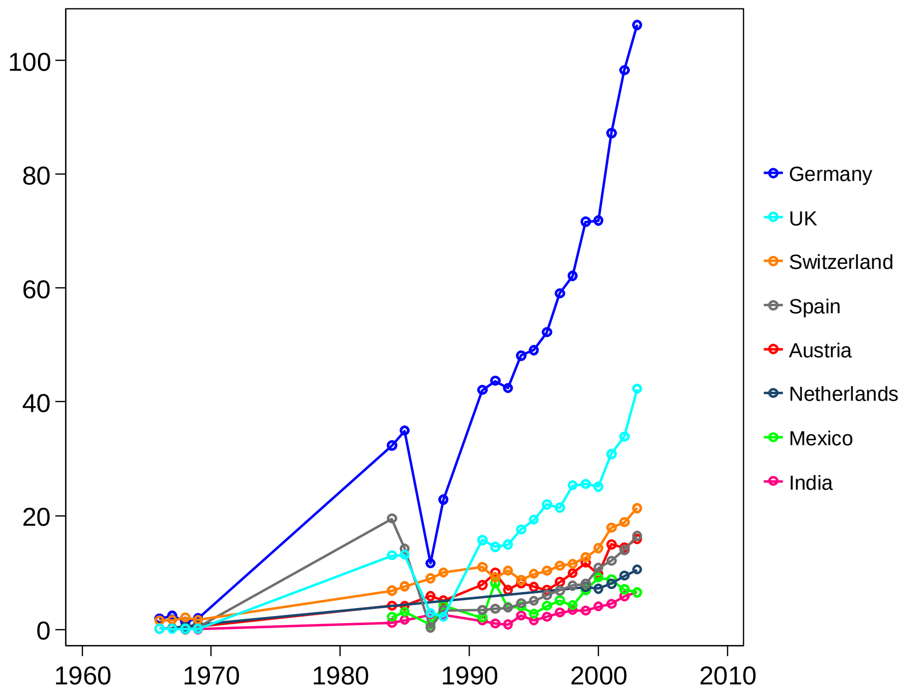

Figure 5.5: **Synthes products sales 1966-2003 by selected countries at royalty base prices (in Mio CHF)**. Country specific data for the years between 1970 and 1985 is missing. Data source: AO/Synthes annual finance reports.

5.3 Impact on Business of Spine/CMF/VET-Medtech industry

Due to a lack of data, it is difficult to disentangle the exact contribution of the different divisions to the overall Synthes sales. Data from 2006 show that the trauma division is clearly the largest contributor in terms of royalty payments, hence sales rates, with about 62% of the royalties, followed by Spine with 22% and CMF with 9%[5] (Source: AO). Regarding market shares, the trauma division has the strongest position with a worldwide market share of 37% in 2016. CMF reaches 27% and Spine 18% (Source: DPS).

[5] «Tools» counts for another 7% but does not correspond to an AO division.

6 Impact on Science (WP4)

Research has been one of the founding pillars for the AO since the beginning. The Laboratory for Experimental Surgery Davos (LESD) was created in 1959. In the first decades of its existence, the LESD increased in size and importance until in 1992 it moved to the newly built facilities in Davos and was renamed AO Research Institute Davos (ARI; [5], [29]). Under this name, it continued its work uninterruptedly until today mainly covering pre-clinical and translational research within the AO.

Simultaneously to the creation of the LESD, the AO created the AO documentation center (AOD) in 1959 as part of the LESD in Davos. Its aim was to register data from all cases treated with the AO method [5]. Yet, the AO documentation center encountered difficulties to reach its aim since the beginning. Its processes and its strategy, that underwent several adaptions, were only partly successful [5]. In 1988 with a change in leadership, the strategy of AO documentation was adapted and from now on supported prospective clinical studies in a decentralized way [5]. After having been located in Bern since 1967 the AO documentation center moved back to Davos in 1992 and was renamed to AO clinical investigation and documentation (CID) in 1998 [30]. In 2001 the CID opened a new branch in Dübendorf and continues to support clinical research, mainly for the internal customers (clinical divisions and institutes).

The AO developed into four divisions, each of which has its own history:

- AOTrauma became a separate division in 2008 [31]. Nevertheless, the focus on trauma constituted the main part of AO research especially in the outset.
- AOSpine: The first pushes for greater autonomy of spine surgeons within the AO occurred in the late 1990s. In 2000, the Board of Directors created an AO Specialty Board for Spine Surgery, which resulted in the creation of a separate division in 2003 [32].
- AOCMF was formally established as a division in 2008 after having been recognized as a separate specialty area already in 1974 [30,33].
- AOVET was established in 1969 and became a separate division in 2007 [30,34].

6.1 Methodological approach of this work package

The impact of AO Research is manifold. One of the main products of AO research is to generate patents and improve surgical processes. This indirect impact of science has been treated in the work packages Education (WP2) and Medtech Business (WP3). Aside from this impact on education and business, AO science also influences other researchers by creating and publishing (clinical) evidence via manuscripts, collaborations, by taking an active part in medical associations or by creating or supporting platforms for scientific exchange. Furthermore, the AO invests substantial funds to further pre-clinical and clinical research in- and outside its walls. Therefore, we measured the impact of the AO on science in four dimensions:

1) Citation trends of core publications
2) Internal and external funding by the AO
3) Collaborations in studies or relationships to universities
4) Fostering the scientific community

From these analyses, AO Invest and AO Development Incubators have been excluded, as they are too recent to be considered for impact analyses.

Citation trends of core publications

Journal publications and books issued by retreated AO researchers were preselected from the literature (for details of search process see attachment chapter 10.4.1). Three AO internal experts were asked to rate these preselected publications for their importance. One expert returned an evaluation. We considered all book publications as well as all journal publications rated as “essential” for further analysis. We treated multiple editions of one book as one publication (e.g. [35] and [36]). Editions in the original language (e.g. German or French) as well as all English editions were taken into account.

Based on a selection of important papers by active AO researchers from ARI and all four divisions, we extracted journal publications that had appeared in journals with impact factors (IF) above 4.0 (in the year of publication). Due to the low median IF of veterinary journals (median IF: 0.86) compared to the other specialities of the AO (e.g. material science/biomaterials: 3.98, neurosciences: 2.91, orthopaedics: 1.63; [37]) we subsequently set the IF-threshold for veterinary journals to ≥2.0.

For CID the first ten entries of the list of most cited papers from the CID database were used to preselect impactful papers. The IF-threshold for further selection of these papers was set at 3.0 for CID-publications.

We used “sum of times cited” from the web of knowledge database from the Web of Science [38] as a measure for number of citations per year. Journal publications were excluded from the analysis if the total amount of citations were ≤5 or if the paper had been published in 2017 (see appendix chapter 10.4.2 and 10.4.3). To compare numbers of citations with other publications in the same field we used highly cited and hot paper thresholds from InCites (see appendix chapters 10.4.5 and 10.4.6).

Internal and external funding by the AO Foundation

The AO Foundation adopts three roles regarding funding: it is (1) a receiver of funds from external sources (e.g. Swiss National Science Foundation), (2) acts as a funder to internal receivers (e.g. ARI, CID, divisions) or (3) funds research at external institutions (e.g. research at Inselspital Bern). In our analyses, we tried to cover all of these roles.

We retrieved data on internal and external funding for LESD and ARI from their annual reports. Missing data could be completed by annual reports from the AO Foundation as well as by ARI and AO Foundation internal data except for the years 1970-1974. Furthermore, we analyzed internal and external funding of clinical research and funding of divisions as well as clinical priority programs (CPP) and mini-grants by means of AO Foundation internal data.

Collaborations

Data of CID collaborations was extracted by the AO from the CID database covering the years 2005 to 2016. Furthermore, we extracted collaborations of ARI from their annual reports from the years 1997 to 2015. Collaborations comprise cooperations within studies as well as university relationships such as assistant professorships, faculty membership, affiliations to universities etc.

Fostering the scientific community

ARI, CID and all divisions were asked to report participation of their employees in boards of scientific or medical associations. Information on conference hosting and the creation of the scientific journal European Cells & Materials (eCM) were extracted from ARI annual reports and literature. We extracted information on the development of the IF-factor of eCM from InCites journal citation reports [37].

6.2 Results

Key findings:

- 25'535 total citations for the 2 most cited core journal papers since 1996
- 9 core papers in the top 1% of highly cited papers in their field in the past 9 years
- A growing number of papers in journals with IFs above 4.0 from 2007 to 2016
- Several early AO books and papers still relevant for research community today
- CHF 289.6 Mio of funding for LESD/ARI 1960 to 2016 and CHF 28.9 Mio of funding for CID 2013 to 2016
- 327 Collaborations within studies and with Universities in the past 19 years.
- ARI: Yearly scientific conference and publication of a scientific journal with an IF above 4.0 since its first classification

Citation Trends of core publications

The early work of the AO funders mainly tried to answer two research questions in biomechanics: whether compression is beneficial for bone healing and if the phenomenon of primary bone healing existed (Schlich [5], S. 88). The results of these research topics lead to the publication of the first two AO books by Müller, Allgöwer and Willenegger "Technik der operativen Frakturbehandlung" in 1963 [39] and its successor "Manual der Osteosynthese" (first edition: [40]). These first books were followed by many other AO book publications also covering AO specifications such as CMF, Spine or VET.

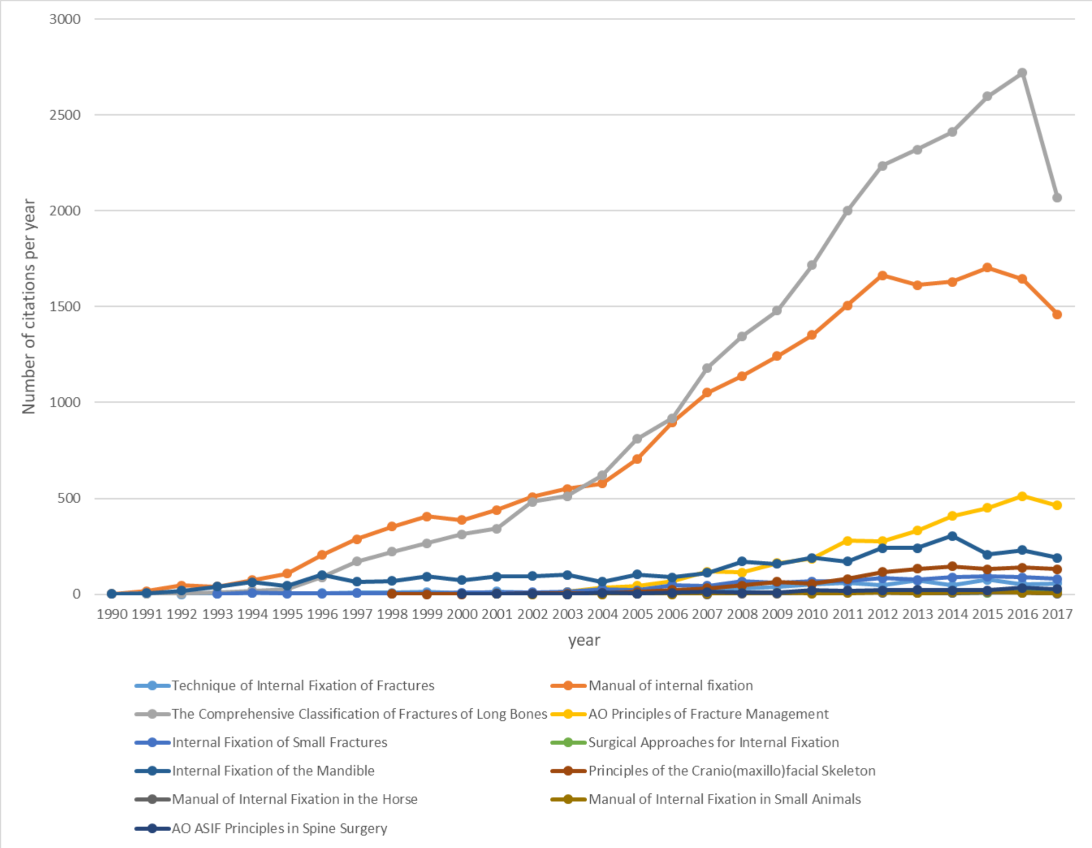

Figure 6.1: **Citation trends 1990-2017 of AO core books**. Source: Web of Science; all editions considered; last update: 30.11.2017; Data is displayed in more detail in the appendix, Figure A6.1.

Today mainly two AO books receive high citation numbers: the “AO Classification of Long Bones” and “The Manual of Internal Fixation” (Figure 6.1). These two books may count as the main legacy of the early years of the AO and according to their citation trends are still relevant for the research community today, even though a certain flattening of the curve can be observed for the “Manual” since 2012. The sharp decline in citations for the “Classification” might be due to incomplete 2017-data in the database. The other AO books, mainly the “AO principles of fracture management”, also keep their influence on research, yet on a rather lower level (for more detail see appendix Figure A6.1).

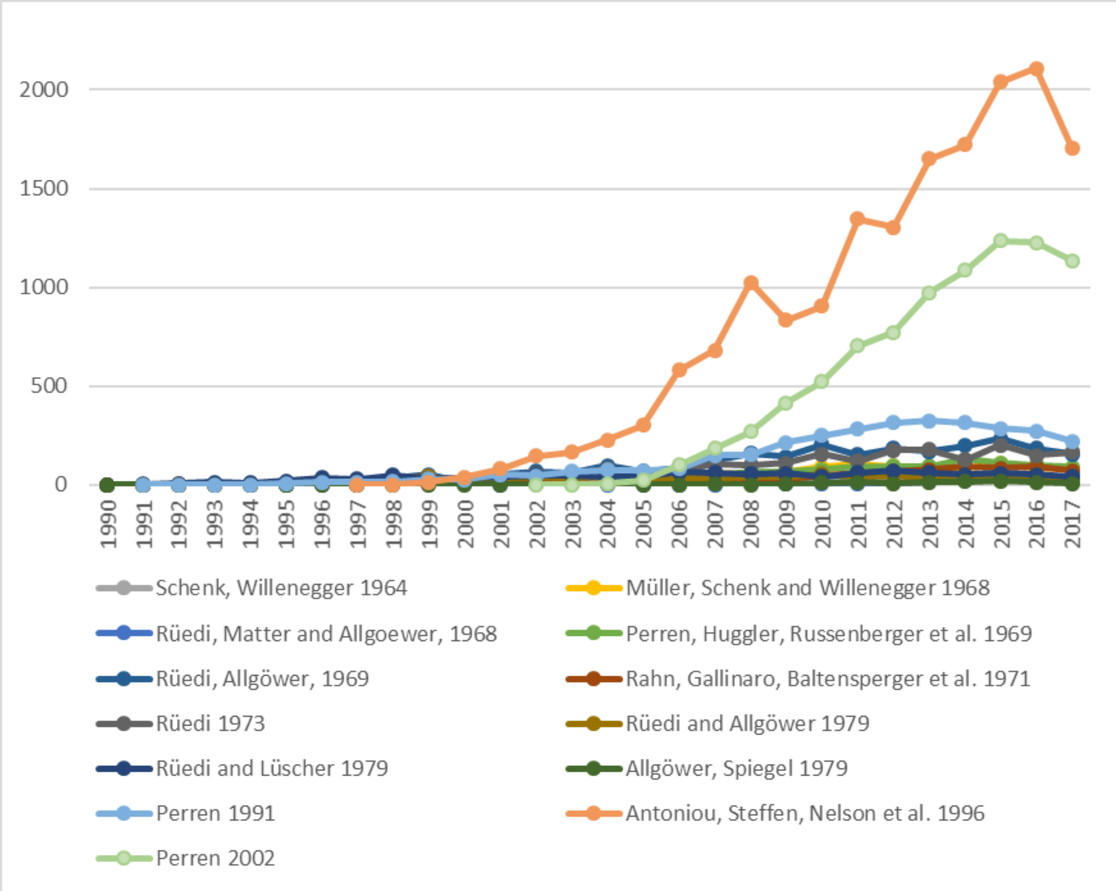

Figure 6.2: **Citation trends 1990-2017 of early AO core papers published between 1959 and 2005**. Including ARI publication from Antoniou et al. 1996. Source: Web of Science; last update: 23.11.2017; data is displayed in more detail in the appendix Table A6.1 and Figure A6.2.

The findings of the AO have, since the beginning, also been published in scientific journals (Figure 6.2). The two most cited papers ([41,42]) would be part of the 1% of most cited papers in the fields of material science or clinical medicine if compared to citation thresholds of highly cited papers of the years 2007 to 2017 (thresholds: sum of citations over the first 10 years after publication: 193 and 218 respectively; see attachment chapter 10.4.5).

For earlier papers from the 1960ies and 1970ties it is more difficult to make a comparison with current citation numbers as the scientific world is fairly different than in the early AO years. Yet, it is noticeable, that many early papers did not entirely lose their significance over the past 50 to 60 years (Figure 6.2; for more detail see appendix, Figure A6.2).

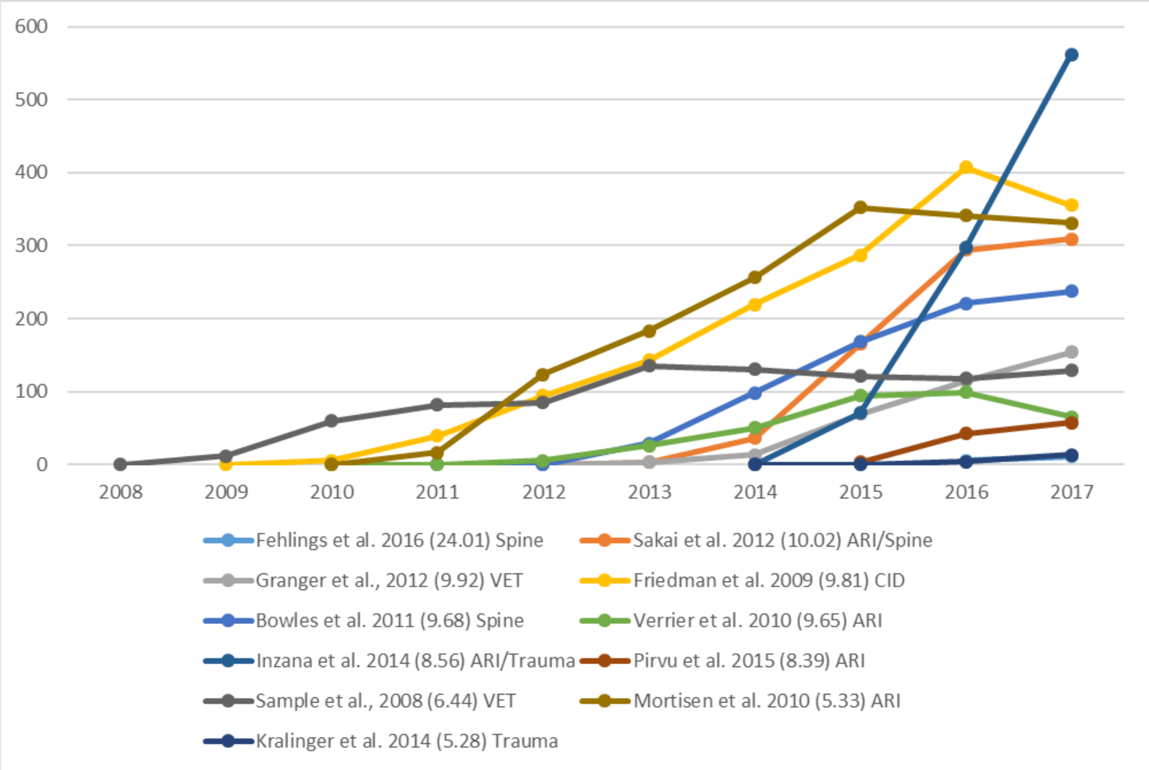

Figure 6.3: **Citation trends of the most influential recent AO journal publications (IF ≥5.0)**. Without ARI publication from Antoniou et al. 1996. Source: Web of Science; Impact Factor in brackets; last update: 23.11.2017; data is displayed in more detail in the appendix: Table A6.2 and Figure A6.6 through Figure A6.10

Nowadays the issues covered by AO research (pre-clinical and clinical research) are much more widespread than in its beginning and cover themes like tissue morphology, disc regeneration, bone infection and regeneration, polymers, stem cells and a wide range of subjects in clinical research. This amplitude in research did, however, not diminish its quality, as nine out of eleven core papers shown in Figure 6.3 meet the high citation thresholds criteria in their field (Figure 6.3, appendix chapter 10.4.5). One paper by Inzana et al. [43] would certainly even meet the criteria of a hot paper as defined by Clarivate Analytics (Figure 6.3; appendix chapter: 10.4.6). Furthermore, the AO researchers were able to publish a growing number of core papers in journals with IFs above 4.0 over the last 10 years (appendix Figure A6.5). This is especially noteworthy as funding of the research units of the AO, at least in pre-clinical research, almost stagnated in the same period (Figure 6.4).

Besides their direct impact on science, AO research results are also used for approval processes. One recent successful example was the case in September 2017, when the

US Food and Drug Administration (FDA) approved a new surgical procedure (Augmented Proximal Femur Nail Antirotation or PFNA augmented) supported by results of a study co-financed by the AO (funded by: AO Foundation, AOTK Trauma, AOTrauma and Depuy-Synthes, data not published yet).

Funding

In its beginning, the funding of the LESD was very modest and mainly covered by external contributions (Figure 6.4). This changed with increasing income from royalties. Over the first decades the budget of the LESD and later ARI increased successively until it started to decrease after 2006/2007 with the new funding structure of the AO. In the past eight years internal funding remained quite stable, whereas the extramural funding could be substantially increased since 2005 (0-5% in the early 2000s to around 20% in the last eight years).

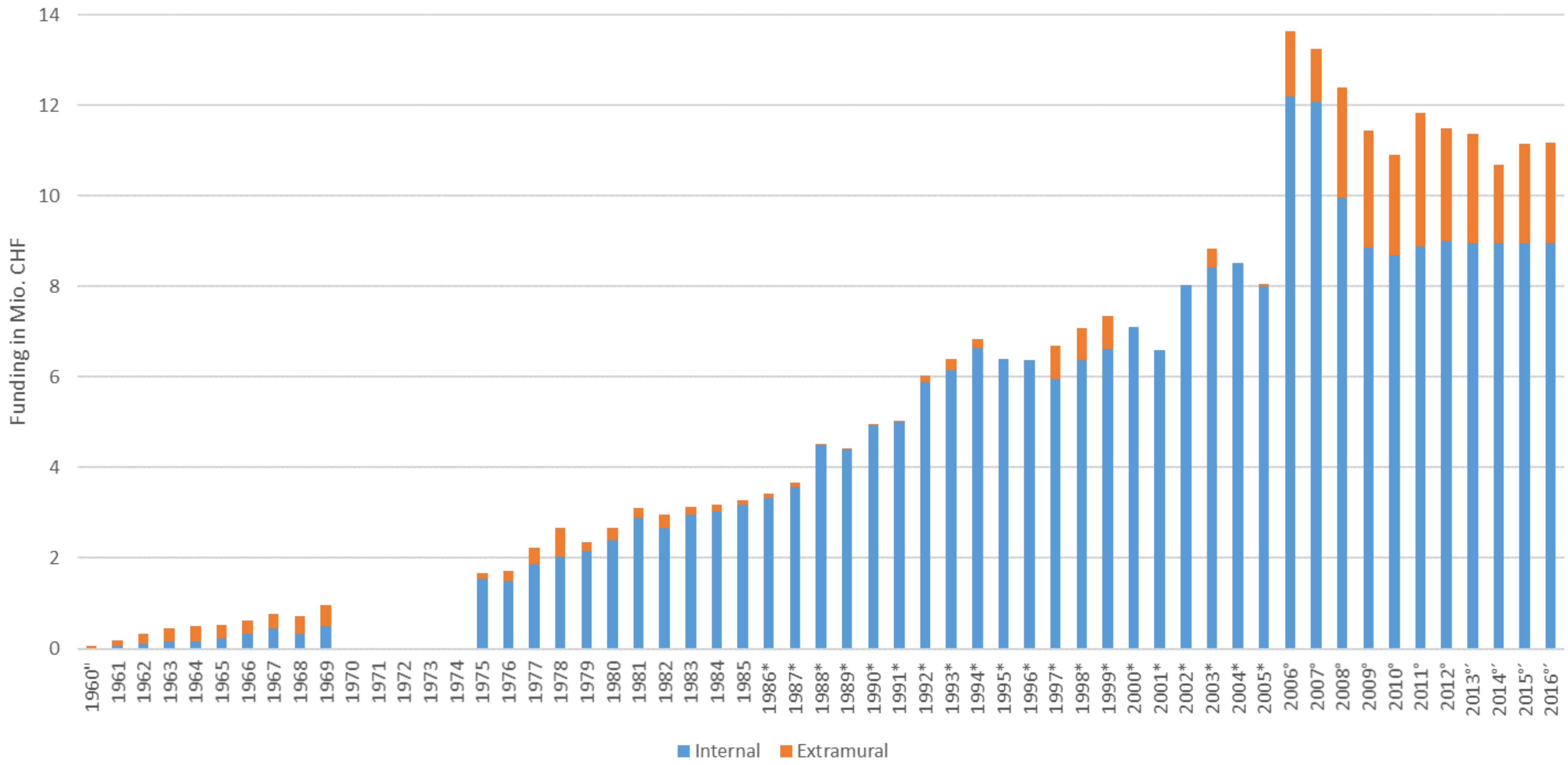

Figure 6.4: **Internal and extramural funding of pre-clinical research by the AO 1960 - 2016**. Sources: annual reports from Laboratory of experimental Surgery Davos (LESD) and AO Research Institute Davos (ARI); '' data of half a year; * source of extramural funding: yearly reports from AO Foundation; ° source: ARI internal data; ´ source for internal funding: AO Foundation internal data

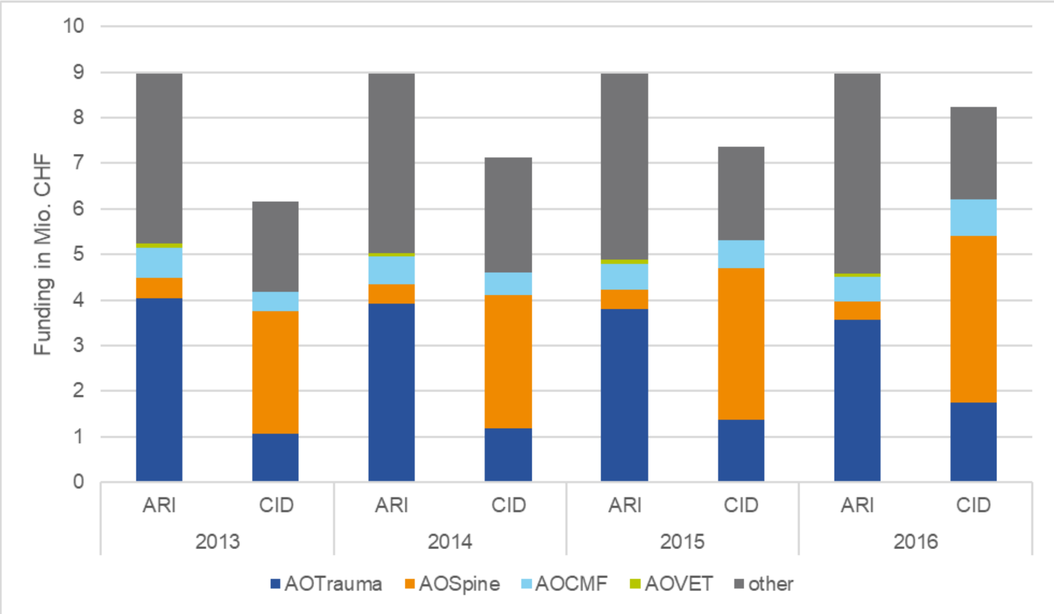

Figure 6.5: **Internal funding of pre-clinical (ARI) and clinical (CID) research by the AO 2013-2016**. Source: AO Foundation internal data; data without administrative costs; category "other" contains AO Foundation, AOTK and AOER for pre-clinical research and AO Foundation and AOTK for clinical research.

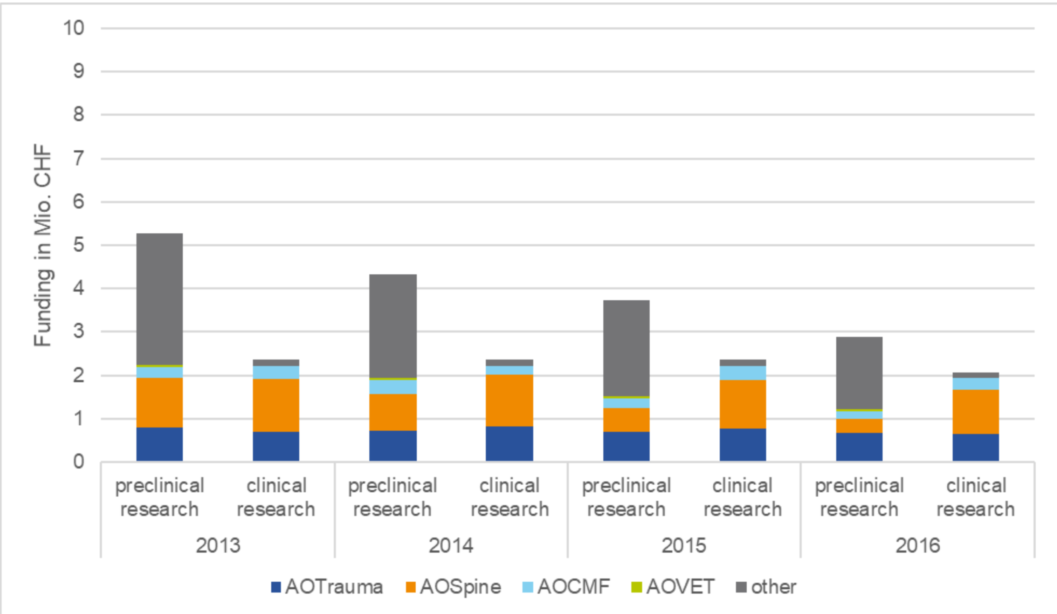

Figure 6.6: **External funding for pre-clinical and clinical research by the AO**. Source: AO Foundation internal data; data without administrative costs; category "other" contains AO Foundation, AOTK and AOER for pre-clinical research and AO Foundation and AOTK for clinical research.

In more recent years a shift in funding from pre-clinical to clinical research can be noticed. Over the past four years the budget of internal pre-clinical research stagnated at almost CHF 9 Mio. per year, whereas the annual internal clinical research budget increased from CHF 6.2 Mio. to CHF 8.2 Mio. in the same period (Figure 6.5). This shift from pre-clinical to clinical research can also be seen in the funding of external partners. Here the amount for pre-clinical research decreased over time (Figure 6.6). It must be assumed, that the impact in science e.g. regarding publications and citation trends will therefore also experience a certain shift in the next few years.

To boost certain research topics the AO defined three clinical priority programs (CPP) so far. The first CPP (2005 – 2015) covered fracture fixation in osteoporotic bones and awarded CHF 6.0 Mio. to external partners. The second CPP (2012 – 2016) focused on bone infections and allocated external partners with CHF 2.6 Mio. The third CPP (patient outcomes) has been approved in 2017 and new studies are currently being planned. Besides CPPs the AO also awards mini-grants e.g. to support multi-centre studies or allocate merit awards. Worldwide 180 such mini-grants amounting to a total of CHF 1.8 Mio. have been awarded by the AO between 2009 and 2017.

Collaborations

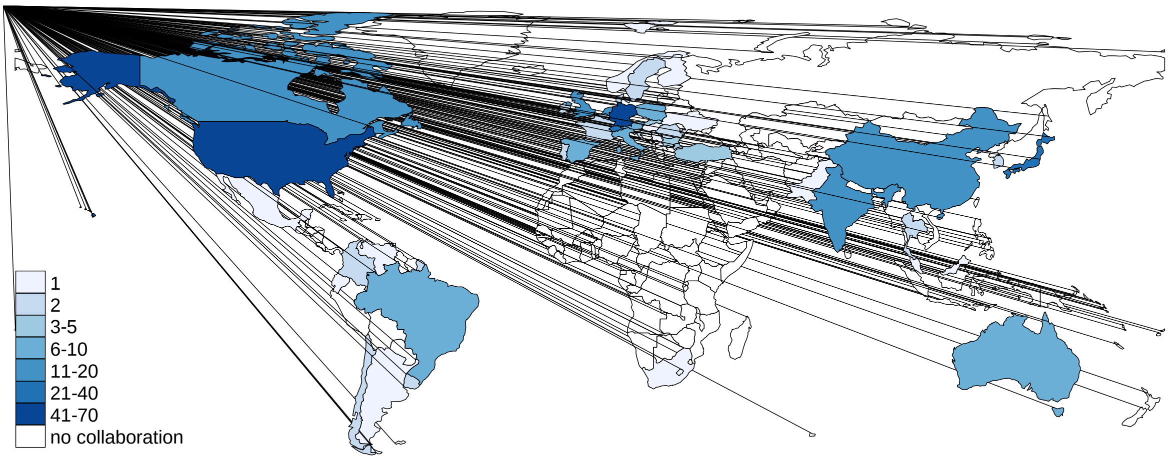

Figure 6.7: **Collaborations of CID and ARI by region.** Source: For CID: Alexander Joeris, AOCID 2005 to 2016, for ARI: Activity reports 1997 to 2015.

Most collaborations shown in Figure 6.7 result from scientific studies lead or supported by CID. Most of these studies were conducted in Europe (111 between 2005 and 2016) in the traditional AO countries, especially in the German speaking ones (58, 52% of European studies). In the Americas the major part of studies took place in the USA (60, 86% of studies North America), whereas Brazil is at the head of the list in South America (6, 38%, of studies South America). In Asia/Pacific Japan (31, 43% of Asia/Pacific studies), China (16, 22%) and India (12, 17%) host most of the CID studies. Only six studies (2.2% of all CID studies) were carried out in the Middle East and only one in Africa (0.4% of all CID studies) so far.

The ARI on the other hand has many links to universities. Some of these ties stem from the origins of the AO, e.g. with several Swiss universities, others have been tied by current ARI staff members more recently. These links mainly cover European sites (19, 73%) but also American sites (6, 23%) and one Australian site (1, 4%).

Fostering the scientific community

AO researchers maintain a broad network and influence the research community by being member of boards of scientific, medical or veterinary associations (35 board memberships from seven current ARI researchers 1990-2017, 20 board memberships from 9 VET members; for details see appendix, 10.4.9 and 10.4.10).

Furthermore, the ARI not only hosted several conferences in Davos (Symposium Biomecanica 1997; European society for Biomaterials 2009; European Orthopaedic research society 2010), it also created its own conference called European Cells & Materials (eCM) in 1999 [29]. From this initiative spurred the idea to create “an online free-to-all scientific journal” with the same name as the conference of which the first volume appeared in January 2001 [29]. Since its first IF attribution in 2008 the eCM journal has had an IF over 4.0 and ranked in the top 10 of its category (Material Science, Biomaterials [37]) until 2015 (Figure 6.8).

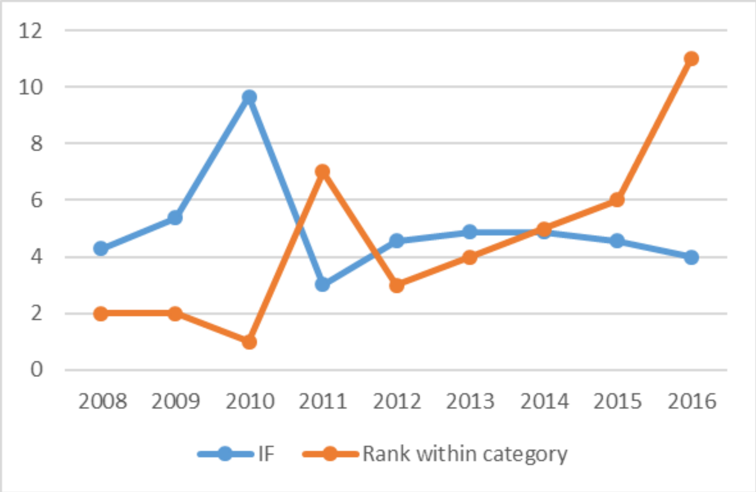

Figure 6.8: **Development of the Impact Factor (IF) and the rank within the Material Science, Biomaterials category of the European Cells and Materials journal**. Source Web of Science [37], last access 05.12.2017

6.3 Impact on Science in Spine, CMF and VET care

Citation Trends of core books and papers

Speciality oriented books of CMF, spine or VET surgery do not achieve citation numbers comparable to the more general publications, yet they are still used in their field of specialisation until today. This is mostly the case for CMF books, where the two main book publications (Manual of internal fixation in the cranio-facial skeleton and Principles of the Cranio(maxillo)facial Skeleton) are still of importance for researchers today (appendix Figure A6.1). For the two other divisions the AO book publications seem to be less used. In journal publications, on the other hand, AO Spine was responsible for most of the high IF publications in the last few years (Figure 6.3; appendix Table A6.2 and Figure A6.9). However, VET not only published in veterinary journals but also in biological/medical journals. IF of biological/medical journals are generally higher than IF of their veterinary counterparts and citation numbers for the four core papers of VET developed accordingly (appendix Figure A6.10). Nothing can be said for citation rates of CMF papers as no core publications have been selected by CMF. CMF preferred to note the top five contributions from the AO that have changed the way surgeons work today (appendix, chapter 10.4.8).

Funding

The total amounts awarded to the three divisions Spine, CMF, VET vary strongly and the differences between the divisions rather widened in the last four years. Spine received most funds, whereas VET received substantially less than the two others (Figures 6.5 and 6.6).

Data on funding also reveals the focus these three divisions pursue in their science: Spine has a clear focus on clinical research, whereas VET is focused on pre-clinical research. CMF is rather balanced between the two foci. Yet, in the last four years, the general shift from pre-clinical to clinical research can also be noticed for the divisions with the exception of VET.

7 Discussion

7.1 Strengths and limitations of the impact evaluation

Impact on patient care:

Our analysis of impact on patient care has several strengths: We used real world patient care data from a large accident insurance company, to describe resource use and costs for state-of-the art fracture care of three index bones in a high-income country (Switzerland). We had also access to historical treatment data for Switzerland (partly form 1958; mostly from 1980 up to 2015: fracture case load; mean direct medical costs per case; mean indirect costs per case [i.e. calculated via length of temporary disability]). Furthermore, we modelled different fracture locations for each of the index bones separately, to account for different clinical courses. We cross-checked the plausibility of the caseload of high impact fractures over years [44] as well as direct medical costs with results of a Swiss NCD study that included injuries. [45]

In addition, we used country specific data for all included 17 high-income countries for population size, health care expenditures, national wages and life expectancy. We validated our findings by cross-comparison with other results (e.g. modelled technology penetration vs. number of teaching events in some countries and vs. sales rates of OS devices; modelled fracture epidemiology with country specific fracture data in the US and NZ)

In summary, our results of impact on patient care represent conservative estimates as we applied conservative assumptions for the input parameters of our model:

- We included only cases with a fracture of an index bone as main diagnosis, as we wanted to isolate the impact on fracture care of the index bone (for example, no cases were included with fracture of an index bone as secondary diagnosis in multi-trauma patients with brain injury, which would have contaminated cost analysis)
- Historical fracture care data and costs, sometimes as early as 1960, were only available for patients younger than 65 years. Thus, we included only such patients

for health economic analysis (exception: direct costs of proximal femur fractures for age group ≥ 70 years)

- Direct medical cost data from the SSUV database, as used for patients treated with osteosynthesis, are a mix of the lower costs of the majority of patients without complications and the higher costs of some (few) patients with complications. Thus, the costs of patients with osteosynthesis and without complications as used in our model are somewhat overestimated. For patients with complications in our model (for OS and for CONS, respectively) we assigned additional costs for treatment of complications.
- For patients beyond working age, we estimated " years of life gained" (YLG) until end of life expectancy. However, patients beyond working age in the age range 65 to 69 years could not be included for this estimation due to lack of specific data. As we had only data for patients older than 70 years, this also leads to an underestimation.
- In working age patients, we used "years of life gained" (YLG) before age 65 years for calculation of productivity gains. Additional YLG in this population (from end of working age until end of life expectancy) could not be used for calculation of indirect cost in our human capital approach. This approach, however, leads to an underestimation of total benefits over the entire expected life span. Thus, we also report the magnitude of YLG from fracture until end of life expectancy in the working age population, to provide a comparable estimate as in the 70+ population. However, to avoid double counting, this total number of YLG must not be simply added to total cost savings.
- Indirect costs do not include unpaid work (i.e. household work; unpaid care of family members; for example, a person aged 70 years with tibia fracture and osteosynthesis may be earlier able to care for children of parents in working age)
- For the estimated impact on the international level, we only included 17 high income countries. Thus, possible effects in other (excluded) high- or middle-income countries (e.g. BRIC-countries: Brazil, Russia, India, China) are not covered. These effects are potentially huge. During the transition process, these middle-income countries have a high burden of injury related morbidity and mortality, for example road injuries with high impact bone fractures. The Global Burden of Disease study [46] estimates this injury burden in the BRIC countries, that is significantly

higher compared to the depicted example high-income countries (Figure 7.1). These data give an impression of possible improvements in different domains in these countries to lower the burden of road injuries: For example, via road safety campaigns and investments in safer infrastructure, as well as via improved access to up-to-date fracture care via osteosynthesis.

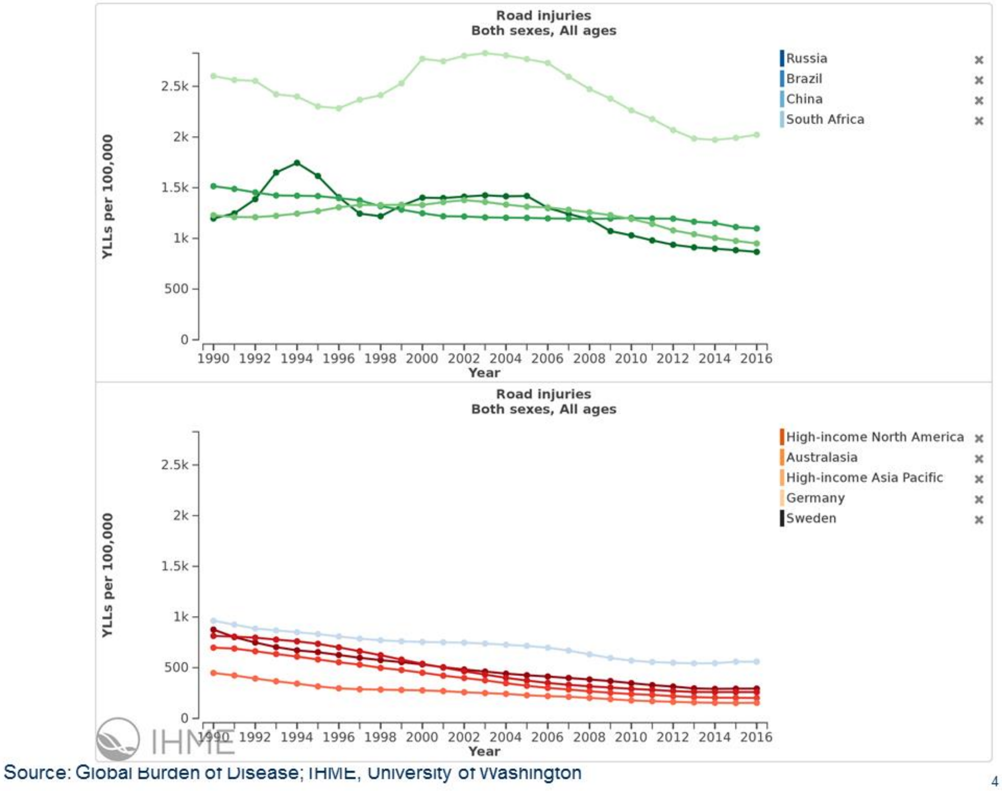

Figure 7.1: **Global Burden of Disease: Road injuries in example high-income countries and BRIC-countries**.

Our modelling approach has several limitations as it is based on critical assumptions:

- The availability of historical cost data in the SSUV data base was sometimes scarce and we assumed 2017 Swiss prices for all years. We validated this approach by inflating retrieved (lower) historic prices to (higher) 2017 Swiss prices via the Health Component of the Swiss consumer price index from 1958 to 2015.
- Coding of diagnoses changed over decades (ICD-8, ICD-9, ICD-10) and calculation mode of some cost elements showed some variation over 60 years (e.g. payments for days off work after injury).
- The workforce of high income countries has changed over time (changing sector mix with decreasing fraction of blue collar and increasing fraction of white collar workers). While this has implications for injury patterns during work time, which is included in the SSUV data, it has also implications for calculation of invalidity rates and success of occupational redeployment. To take this into account in our sensitivity analysis, we have varied invalidity rates towards lower values which reflects a higher degree of white collar workers.
- We used fracture specific cost data for Switzerland, but no such national data were available in the same granularity for the other high income countries.
- From the year 2000 onwards we assumed a technology penetration rate of 100% in all included high income countries. This may not always and in all regions be the case, as studies about regional variations in health care systems have shown empirically. [47]
- In addition, complication rates may differ substantially depending on regional case mix and surgeon case load.[48] We had no specific data to take these factors into account in our study.
- For some country features, we assumed similar conditions over time for all included high income countries as in Switzerland (i.e. change of age structure of population; epidemiology of changes in fracture incidence over time).
- Organisational and financial responsibilities in a health care system may differ across countries. For example, our approach is derived from the perspective of a social insurance based health care system. Such a perspective is not valid for the whole observation period for some countries (e.g. mostly private health insurance system of the USA, until the Affordable Care Act in 2012).

Impact on education:

As always, strength and limitations go hand in hand. Regarding the impact of the AO's educational activities, we can provide a full account of the number and participants of the AO Davos Courses, the AO's flagship educational activity over the past 60 years. In addition, we provide a complete summary on the amount of the worldwide courses the AO carried out in that period and their regional development such as the first course in a particular country. Since 1960, 65'000 surgeons have been trained in the AO Davos Courses, 580'000 surgeons received training in one of the local AO courses, and 7'800 surgeons participated in the fellowship program. This shows the large educational engagement of the AO since its beginnings, which certainly provided the basis for the success of the diffusion of the "AO-Technique" and of the successful spread and acceptance of osteosynthesis as a standard technique in general.

Besides the courses, the textbooks provided an important means of knowledge transmission. In the early years, they complemented the courses, where the focus was on training the "hands-on" skills. More recently, online materials such as videos, online courses, and, in particular, the AO Surgery Reference, have become very important resources for surgeons performing osteosynthesis and for fracture care in general. However, as we had only very limited data on the use of these resources over time, we refrained from an in depth analysis. Nevertheless, these types of educational activities are certainly of essential importance and will play a leading role in the future – as did the classical courses in the past 60 years.

Impact on business:

Regarding the AO's business impact our analyses show strengths but also limitations. We had difficulties to find sales figures of products directly related to the AO over time. Nevertheless, we are in the position to give an account of the detailed development of Synthes sales over the past 60 years. Synthes was the brand under which various producers sold the products developed by and for the AO. Until 2006, the AO was owner of all Synthes patents and owned the label. Synthes sales of all producers from 1961 to 2005 sum up to CHF 11,6 Billions (at royalty base prices, final prices may be 10 to 50% higher). The sales of Synthes US and Synthes Inc., the latter being the company resulting from the merger of all previously independent producers, amount for 1975 to 2016 to CHF 54’465 Mio (at final prices). Overall figures are mainly driven by the sales in recent years, as sales increased exponentially over time. This shows that AO products have been and still are highly demanded. While in the early years, the AO producers where often the only osteosynthesis material producer in a particular country, competitors soon appeared and took their share of the market – despite the AO’s initial efforts to fight imitations of their products. However, still today Synthes has a market share of more than one fourth in the worldwide trauma market.

The following limitations apply: Because we have no data on the various production sites of the Synthes producers, on imports and exports, nor on the value added at a particular location, it was not possible to estimate a specific regional economic impact of the Synthes production. Nevertheless, qualitative evidence, especially the prosperous development of the original Synthes producers Mathys and Straumann, one of the early medtech companies in Switzerland, indicate that the AO has had an important impact on the early development of the medtech sector in Switzerland. But it must be kept in mind, that the production sites in other countries such as Germany or the US, soon had a larger output than the original Swiss production sites.

Impact on science:

Our analysis of the impact of the AO on science has several strengths and limitations: We could provide citation trends of all important book publications of the AO. In terms of paper publications, on the other hand we mostly used a list of papers estimated as important by current and former AO employees and only considered high IF-publications for further analysis instead of using the entire AO publication list. This process might have led to the exclusion of papers with high citation numbers. Therefore, these analyses can be considered as rather conservative. Citation trends of several AO books and papers did show high numbers of citations per year or overall citations if compared to other papers in their research fields and hence demonstrate their influence on researchers. This is even true for some very early AO publications. All departments and divisions, that provided us with data, did contribute papers that have been published in high IF journals and did meet high citation thresholds regardless of their size or orientation. The total number of citation of the two most cited AO core papers was 25’535. In addition, AO researchers were able to publish a growing number of core papers in journals with IFs above 4.0 over the past 10 years.

Overall these analyses show that the AO does impact the science community in all their fields of research. However, because of its thematic breadth from basic research over clinical research to development of new techniques and patent deposition, it is difficult to compare the AO science departments to other institutions such as Universities, University clinics or to R&D departments of firms and therefore cross-validate our results. In addition, citation-based measures are only an indicator of impact and represent a researcher-based view. [9]

For LESD/ARI we provided data on funding since 1960 with the exception of a few years in the early 1970ies. The LESD/ARI received a total of CHF 289.6 Mio over the 52 years covered by our analyses. Due to missing data we could not provide the same analysis for clinical research. Nevertheless, data on the past four years revealed certain trends within AO research, e.g. a shift towards more clinical research. It must be assumed that this shift will also be felt in the output of CID/ARI in the coming years. Even if funding of research projects does not represent a direct impact on science per se, it has been necessary to build the foundation of the success the AO ideas did and do generate in the scientific and clinical world.

The AO also maintains a rich network within the science community. This is represented not only by their presence in several boards of medical, scientific or veterinary associations, but also by their collaborations with many clinics and Universities. Furthermore, the AO maintains its own platforms in terms of a yearly conference and a scientific journal with an IF above 4.0 since its first classification. These links to other researchers and clinicians and their institutions furthers the impact on science as a whole.

7.2 Significance of impact on patient care

The potential net benefit of OS for fractures in the three index bones in 17 high income countries over 60 years is CHF 855 bn (base case; population age <65; 3% discount rate; in 2015 Swiss Francs).

Such an estimate is difficult to understand, as cognitive references are often made to a specific country, a specific time window (often1 year) or a benchmark (e.g. direct medical costs of specific diseases or the gross domestic product, GDP, of a country).

To break our figures down, we have made some comparisons as depicted in Table 7.1. To evaluate the impact of medical innovation, a research group from the US has assessed the value of antihypertensive drugs in preventing subsequent morbidity and mortality in US-American persons with high blood pressure. [7] The researchers assessed the impact of better controlled blood pressure on coronary heart disease (CHD; myocardial infarction) and on cerebrovascular disease (CVD, stroke) calculating savings in direct medical costs. In addition, they quantified the number of deaths avoided due to better controlled blood pressure.

Comparing our figures with this impact evaluation, we can make the following comparisons:

In terms of excess deaths avoided, the annual impact of osteosynthesis on proximal femur fracture care in the US is in a similar dimension as the annual impact of antihypertensive care in the US (osteosynthesis: 2’600 lifes saved [population age: <65 years] plus 126’000 lifes saved [population age: ≥70 years]; antihypertensive drugs: 86’000 lifes saved [population age: 30-79 years]).

For comparison of cost savings, we used our combined estimates (femur, tibia and radius fractures; all locations; direct and indirect costs; population age <65 years). The impact of osteosynthesis in the US in the year 2002 is again in a similar dimension as the annual impact of antihypertensive care in the US (osteosynthesis: 14.0 bn US$ saved; antihypertensive drugs: CHD: 5.8 bn US$ saved; CVD: 10.7 bn US$ saved; population age: 30-79 years). However, the annual savings due to antihypertensive drug in the US may be substantially underestimated in our comparison, as no indirect costs were included. [7]

A tabulation of savings compared to the GDP may also be useful. The estimated cost savings for osteosynthesis and for antihypertensive drugs are in a comparable range when compared with the GDP of some example countries (antihypertensive drugs for CHD or CVD: USA 0.05 to 0.09% of GDP in 2002; OS for fractures: USA, Switzerland and Germany: 0.06% to 0.08% of GDP in 2016).

Technology	population	time span	impact on	cost category	country	year	result		
antihypertensive drugs	30-79 yr	1 year	excess deaths from CVD	intangible costs	USA	2001	86000	lifes saved	
OS for femur & tibia fractures	<65yr	1 year	avoided excess deaths from fracture	intangible costs	USA	2001	2606	lifes saved	
OS for proximal femur fracture	70+ yr	1 year	avoided excess deaths from fracture	intangible costs	USA	2001	126114	lifes saved	
									% of GDP*
antihypertensive drugs	30-79 yr	1 year	expenditures CHD	direct medical costs	USA	2002	5.8	bn US$ saved	0.05%
antihypertensive drugs	30-79 yr	1 year	expenditures CVD	direct medical costs	USA	2002	10.7	bn US$ saved	0.09%
OS for femur, tibia, radius fractures (all locations)	<65 yr	1 year	expenditures fracture	direct & indirect costs	USA	2016	14.0	bn CHF saved	0.08%
					CH	2016	0.40	bn CHF saved	0.06%
					GER	2016	3.1	bn CHF saved	0.07%

Table 7.1 Context of study results. Comparison of our findings are given (1) with an impact evaluation on antihypertensive drugs in preventing subsequent morbidity and mortality in US-American persons with high blood pressure [7] and (2) with gross domestic product of some example countries. *% of GDP (gross domestic product): the ratio was calculated as follows: savings (in CHF) / GDP (in CHF after conversion from US$) of the respective country for the specific year (source data: OECD). CVD: cerebrovascular disease; CHD: coronary heart disease.

7.3 Synergistic effect of Education, Business and Science

The three domains education, business and science have been treated separately in our report. However, since the beginning of the AO these three domains mutually enriched and reinforced one another. Basic results from science were needed to further the acceptance of the osteosynthesis technique among peers without which neither education nor business would have developed as shown in this study [5]. Yet, only the closely-knit ties developed in education and the closeness to clinical work could also develop the knowledge and educated manpower that were the basis for further developments in science and the demand for the AO tool set which furthered business.

This interplay between these three domains was not a result of pure chance. It has been designed by the funders of the AO quite from the beginning. Urs Heim (2012) is citing Maurice Müller by mentioning the four pillars of the AO as being: Instrumentation, Research, Documentation and Teaching [49]. Even though we treated documentation as part of research in our report, we believe, that only the synergistic effect of these domains could generat the impact detected in our study. The combined approach chosen by the funders lead to an overall impact that each domain alone could not have yielded by itself.

7.4 Future challenges and projects

The technology of osteosynthesis is well established in state-of-the-art fracture care. The impact on patient care, on education, the medtech industry and on science has been assessed in this report. However, as with any technology, new questions arise and old problems are to be resolved.

In the clinical domain, such future prospects may cover several areas:

- Re-evaluation of the evidence base: Studies that evaluate (1) if osteosynthesis leads to better results compared to conservative therapy in some fracture types, where indication for surgery is under debate or (2) which approach of osteosynthesis is more effective, where the indication for surgery is non-controversial. This is a cornerstone of evidence based health care and RCTs are under way.[50]

- Technological innovations with value for patients: Device infection and device failure are still complications with high impact on patients' quality of life. Despite the great improvements made in development of high-tech implants in recent years, evolution of technical progress may further provide useful innovations (e.g. concerning disc regeneration, bone regeneration, polymers, stem cells) and even more effective strategies to prevent device infection.
- Evaluating the impact of educational activities on the surgeon‘s performance and consecutively on the improved of patient outcome.

From a population health perspective, the knowledge base for health services research has to be improved: [51]

- Improved availability of real world data in fracture care
- Standardised assessment of quality of life (QOL: EQ-5D instrument) and patient reported outcome (PRO) over time after osteosynthesis to assess patient benefit
- Implementation and availability of data from real world registers (OS-rates, e.g. for radius fractures; QOL; PRO; complications; mortality)
- Combination of patient benefit data and costs to assess real world cost-effectiveness of OS ("value of health care"; may be in cooperation with large national injury insurance companies)
- Impact assessments: Do clinicians comply with current guidelines?
- Continuous monitoring of impact indicators in fracture care

7.5 Conclusions

Based on the data available in this report, the technology of osteosynthesis had a significant impact on patient care after bone fractures over the last 60 years.

Improved functional results with higher return to work rates, as well as decreased mortality rates after long bone fractures had a dramatic impact: Osteosynthesis lead to significant productivity gains for society and saved a substantial amount of life years.

This impact was multiplied by the interdependence of three additional factors: The structured education of numerous surgeons to apply this technology, the rise of a Medtech industry in orthopaedics and the stepwise development of the scientific knowledge base of surgical fracture care, as assessed in our report. This virtuous cycle enabled a spread of this technology to many countries word wide.

Thus, osteosynthesis developed to the state of the art for treatment of a wide range of fracture types and has increased value of health care.

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Declarations

Competing interests: The authors KE, MH, FM, FK and BU declare that they have no competing interests.

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55. Clement ND, Beauchamp NJ, Duckworth AD, McQueen MM, Court-Brown CM: The outcome of tibial diaphyseal fractures in the elderly. Bone Joint J 2013; 95-B: 1255-62

56. McNamara IR, Smith TO, Shepherd KL, Clark AB, Nielsen DM, Donell S, Hing CB: Surgical fixation methods for tibial plateau fractures, Cochrane Database of Systematic Reviews, John Wiley & Sons, Ltd, 2015

57. Scholz-Odermatt S: Veränderung der Unfallpyramide, Unfallstatistik UVG 2008-2012. Edited by Suva. Luzern, Switzerland, 2012, pp 71-79

10 Appendix

10.1 Appendix of WP1 (Patient Care)

10.1.1 ICD-10 codes

ICD-10 for femur fractures:
S72.0 Fracture of head and neck of femur
S72.1 Pertrochanteric fracture
S72.2 Subtrochanteric fracture of femur
S72.3 Fracture of shaft of femur
S72.4 Fracture of lower end of femur
ICD-10 For tibia fractures:
S82.1 Fracture of upper end of tibia
S82.2 Fracture of shaft of tibia
S82.3 Fracture of lower end of tibia
S82.5 Fracture of medial malleolus
ICD-10 For radius fractures:
S52.1 Fracture of upper end of radius
S52.3 Fracture of shaft of radius S52.5 Fracture of lower end of radius

Table A3.1: **ICD-10 codes for fractures of index bones**

10.1.2 Structure of decision tree

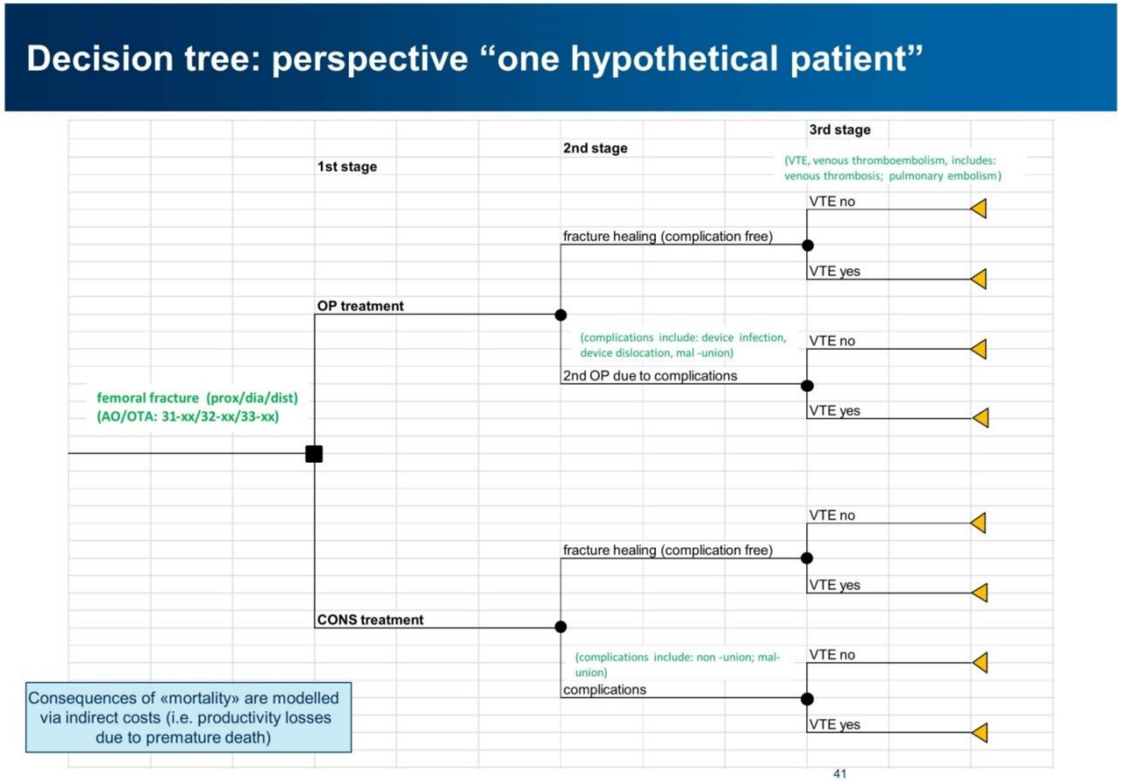

Figure A3.1: **Structure of decision tree for analysis.** An example is given for femur fractures.

10.1.3 Consumer price index in Switzerland

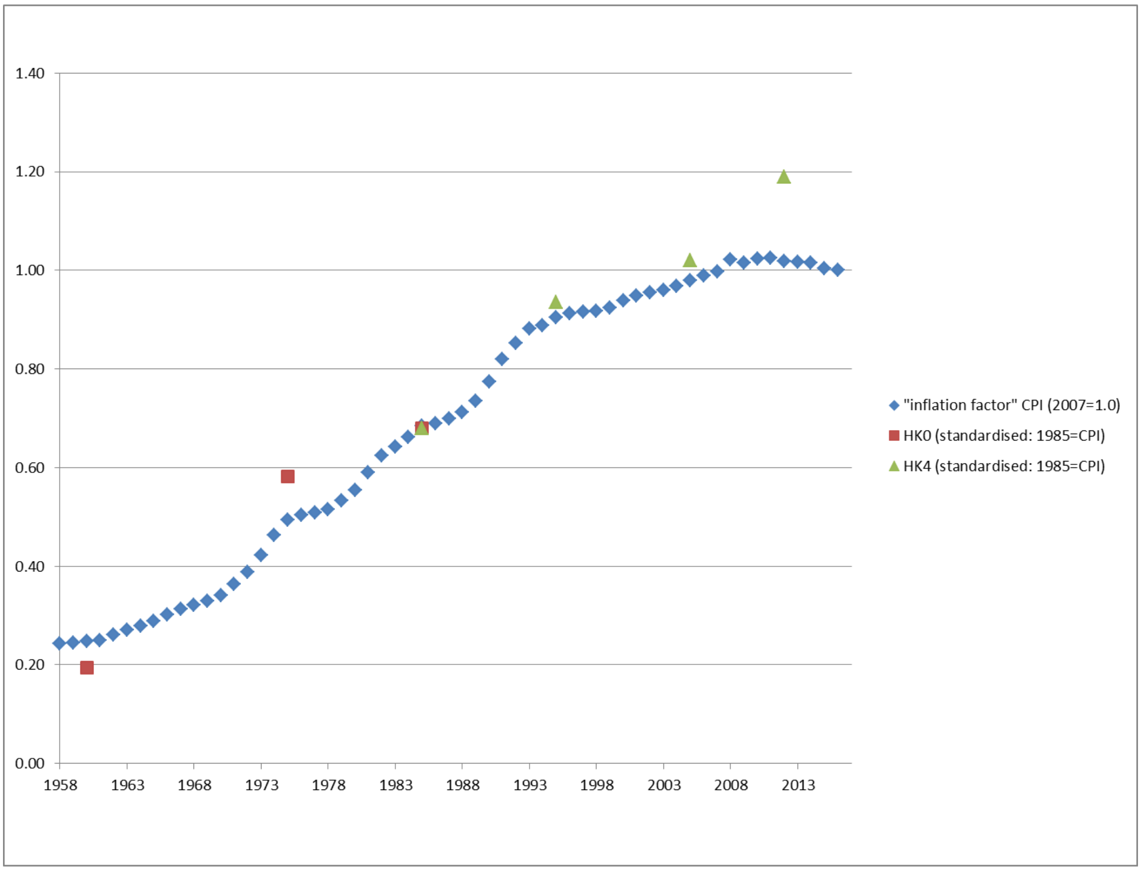

Figure A3.2 Historical cost data for fracture management and Health Component of the Swiss consumer price index go hand in hand over the last 60 years. An example is given for costs of femur fractures (any location). Cost data and consumer price index (CPI; 2007=1.0) are depicted from 1958 to 2015. Red squared data points represent treatment costs in the first year after injury (HK0; from 1959 to 1985; standardized to 1985=CPI). Green triangled data points represent treatment costs in the first four years after injury (HK4; from 1985 to 2015; standardized to 1985=CPI). No historical cost data were available for HK4 before 1985.

10.1.4 Country specific factors

	Europe											North-America		Asia/Pacific				
	Reference																	
17 Countries	Schweiz	Deutschland	Österreich	Belgium	Netherlands	Luxemburg	United Kingdom	Denmark	Norway	Sweden	Finland	USA	Canada	Japan	Korea*	Australia	New Zealand	
	SUI	GER	AUT	BEL	NED	LUX	GBR	DEN	NOR	SWE	FIN	USA	CAN	JPN	KOR	AUS	NZL	
inhabitants (n)	8139631	80425820	8426311	11047740	16754960	530946	62858800	5591572	5019000	9519374	5413000	314112100	34880490	127515000	50004440	22728000	4408100	Stand 2012
pop_fact	1	9.88076978	1.03522027	1.35727774	2.05844221	0.06522974	7.722561379	0.68695645	0.61661272	1.16950928	0.66501786	38.59045944	4.28526674	15.6659436	6.14333008	2.79226417	0.54156018	
HC expenditures (pp USD PPP)	6325	4819	4553	4256	5131	4371	3235	4553	5862	4904	3442	8713	4351	3713	2275	3866	3328	Stand 2013
HCE_fact	1	0.762	0.720	0.673	0.811	0.691	0.511	0.720	0.927	0.775	0.544	1.378	0.688	0.587	0.360	0.611	0.526	
life expectancy (years)	82.9	80.9	81.2	80.7	81.4	81.9	81.1	80.4	81.8	82	81.1	78.8	81.5	83.4	81.8	82.8	81.4	
lexp_fact	1	0.976	0.979	0.973	0.982	0.988	0.978	0.970	0.987	0.989	0.978	0.951	0.983	1.006	0.987	0.999	0.982	
GDP per person (USD not PPP)	63739	48990	50688	46701	51285	103352	43124	49810	59350	49410	43364	57591	44025	41534	35751	47770	38833	Stand 2016
wage_fact	1	0.769	0.795	0.733	0.805	1.621	0.677	0.781	0.931	0.775	0.680	0.904	0.691	0.652	0.561	0.749	0.609	
tech penetration																		
p_OP (TEXT)	reference	5 years delay	5 years delay	10 years dela	10 years dela	10 years dela	10 years delay	10 years dela	10 years dela	10 years dela	10 years dela	25 years delay	25 years delay	25 years dela	25 years dela	25 years dela	25 years delay	

Table A3.4: Parameters of 17 high income countries for calculation of each of the five country specific factors.

10.1.5 Key input parameters of economic model

	age group	**initial therapy**	**complication**[1]	**absence from work** [2] (after complication in stage 2)	**VTE** [3] (without complication in stage 2)	**VTE** [3] (after complication in stage 2)	**mortality**
stage of model		stage1	stage 2	stage 2	stage 3	stage 3	overall
type of parameter	years		p event	months	p event	p event	p event
femur fracture proximal	<65	OS	0.06	6	0.05	0.08	0.003
		CONS	0.05	155	0.10	0.20	0.03
	>70	OS	0.06		0.05	0.08	0.27
		CONS	0.05		0.10	0.20	0.60
femur fracture shaft	<65	OS	0.05	12	0.05	0.08	0.003
		CONS	0.05	373	0.10	0.20	0.03
femur fracture distal	<65	OS	0.05	5	0.05	0.08	0.003
		CONS	0.05	376	0.10	0.20	0.03
tibia fracture proximal	<65	OS	0.05	5	0.05	0.08	0.001
		CONS	0.05	274	0.10	0.20	0.01
tibia fracture shaft	<65	OS	0.05	7	0.05	0.08	0.001
		CONS	0.05	299	0.10	0.20	0.01
tibia fracture distal	<65	OS	0.05	9	0.05	0.08	0.001
		CONS	0.05	279	0.10	0.20	0.01
radius fracture proximal	<65	OS	0.13	2	0	0	0
		CONS	0.05	60	0	0	0
radius fracture shaft	<65	OS	0.05	3	0	0	0
		CONS	0.05	61	0	0	0
radius fracture distal	<65	OS	0.05	3	0	0	0
		CONS	0.05	52	0	0	0

Table A3.5: Key input parameters of decision tree model. Grey shaded data are subject to sensitivity analyses.

OS: osteosynthesis; CONS: conservative therapy; VTE: venous thromboembolism (includes deep vein thrombosis; pulmonary embolism); data are derived from literature (for complications [21,50,52-56], for VTE [56], for mortality [15,16,57]), from SSUV-database [24] (for absence from work; mortality) and from expert opinion.

[1] Complications of OS in stage 2 include: device infection, device dislocation, non-union; complications of CONS in stage 2 include: non-union; mal-union;

[2] Absence from work for OS and CONS: intermediate or permanent absence from work due to complication in stage 2 (for example: scenario OS: patient with femur shaft fracture [mean age 34 yr.] with OS treatment and complication non-union: assumed revision surgery with new implant and overall 12 months absence from work after injury; scenario CONS: Same 34 year old patient with femur shaft fracture with CONS treatment and permanent non-union: assumed 373 months absence from work for the remaining period until age 65, corresponding to 100% invalidity)

[3] For VTE, two scenarios were modelled: probability of VTE without prior complications in stage 2 and probability of VTE after prior complications in stage 2 (for example: patient with femur shaft fracture [mean age 34 yr.] with OS treatment and second OS due to device infection: probability of VTE is assumed 8% compared to 5% in case of complication free fracture healing without second surgery).

fracture case load (cases per year in Switzerland)	age group (years)	1958	2017	data source
femur fracture proximal	<65	300	650	SSUV
	>70	4000	12500	Medstat
femur fracture shaft	<65	1480	170	SSUV
femur fracture distal	<65	87	515	SSUV
tibia fracture proximal	<65	310	2042	SSUV
tibia fracture shaft	<65	1666	405	SSUV
tibia fracture distal	<65	170	731	SSUV
radius fracture proximal	<65	654	905	SSUV
radius fracture shaft	<65	515	119	SSUV
radius fracture distal	<65	3682	4429	SSUV

Table A3.6: Case load of fractures in Switzerland as input parameters of decision tree model. “Cases UVG” are derived from SSUV-database [24] and “cases KVG” from Medstat [14], missing data were extrapolated via expert opinion.

UVG: Swiss National Accident Insurance Law; KVG: Swiss National Health Insurance Law

10.2 Appendix of WP2 (Education)

No additional files.

10.3 Appendix of WP3 (Business)

No additional files.

10.4 Appendix of WP4 (Science)

10.4.1 Description of searching procedure for the preselection of early AO journal publications

Aim of the search: reveal core journal publications of the AO with a focus on the earlier years.

Details of the search:

- Title screening of reference lists of the following publications:
  - Perren SM. Evolution of the internal fixation of long bone fractures. The scientific basis of biological internal fixation: choosing a new balance between stability and biology. 2002
  - Schlich T. Surgery, Science and Industry: A Revolution in Fracture Care, 1950s–1990s. 2002
  - Ruedi TP, Murphy WM, Moran C. AO Principles of Fracture Management, Vol. 1. 2nd edition, 2007
  - Ehrenfeld, M., Manson, P.N., Prein, J. Principles of internal Fixation of the Craniomaxillofacial Skeleton. 2012: only Chapter 1.3.3.
- Titles were screened:
  for authors: Allgoewer M, Mueller ME, Perren SM, Rahn BA, Schatzker J, Schenk R, Tepic S, Willenegger H.;
  for basic AO research themes such as primary bone healing etc as well as
  for basic papers on plates and screws.
- Not included were papers on adverse outcomes such as non-union, pseudoarthrosis etc. as well as AO publications before 1958 and after 2005

The three AO internal experts who were asked to rate each paper for its importance were explicitly asked to add missing core publications to this initial list.

Furthermore, four papers by Ruedi TP (et al.) mentioned as core papers by current AO employees were also added to the list of early papers (Table A6.1).

10.4.2 Early AO core papers rated as essential by J. Prein

Year	Journal	Authors	Title	Total Citations °
1962	Langenbecks Arch Klin Chir Ver Dtsch Z Chir	Willenegger H, Schenk R, Straumann F, Müller M, Allgöwer M, Krüger H.	Methodik und vorläufige Ergebnisse experimenteller Untersuchungen über die Heilvorgänge bei stabiler Osteosynthese an Schaftfrakturen	1
1963	Langenbecks Arch Klin Chir Ver Dtsch Z Chir	Allgoewer M, Mueller ME, Schenk R, Willenegger H.	Biomechanische Prinzipien bei der Metallverwendung am Knochen	6
1964	Langenbecks Arch Klin Chir Ver Dtsch Z Chir	Schenk RK, Willenegger HR.	Zur Histologie der primären Knochenbruchheilung	427
1968	Helv Chir Acta	Müller J, Schenk R, Willenegger H.	Experimentelle Untersuchungen über die Entstehung reaktiver Pseudarth-rosen am Hunderadius	1'298
1968	Helv Chir Acta	Rüedi TP, Matter , Allgoewer M.	Die Intrartikularen Frakturen des distalen Unterschekelendes	181
1969	Acta Orthop Scand Suppl	Perren SM, Huggler A, Russenberger M, Allgöwer M, Mathys R, Schenk R, Willenegger H, Müller ME.	The reaction of cortical bone to compression.	1'236
1969	Injury	Rüedi TP, Allgoewer M.	Fractures of the lower end of the tibia into the ankle-joint.	2'453
1971	J Bone Joint Surg Am	Rahn BA, Gallinaro P, Baltensperger A, Perren SM.	Primary bone healing. An experimental study in the rabbit	905
1973	Injury	Rüedi TP.	Fractures of the lower end of the tibia into the ankle joint: results 9 years after open reduction and internal fixation.	2'049

Table A6.1: **Early AO journal publications.** Either rated as essential by J. Prein, or mentioned as core paper by current AO employees. Ordered by year of publication; ° Source: Web of Science.

Year	Journal	Authors	Title	Total Citations
1979	Clin Orthop Relat Res	Allgower M, Spiegel PG.	Internal fixation of fractures: evolution of concepts	774
1979	Clin Orthop Relat Res	Rüedi TP, Allgöwer M.	The operative treatment of intra-articular fractures of the lower end of the tibia.	1'134
1979	Clin Orthop Relat Res	Rüedi TP, Lüscher JN.	Results After Internal Fixation of Comminuted Fractures of the Femoral Shaft with DC Plates	134
1991	Injury	Perren SM, Buchanan JS.	The Concept of Biological Plating Using the Limited Contact-Dynamic Compression Plate (LC-DCP). Scientific Background, Design and Application	3'286
2002	J Bone Joint Surg Br	Perren SM.	Evolution of the internal fixation of long bone fractures. The scientific basis of biological internal fixation: choosing a new balance between stability and biology.	8'659

Table A6.1 (continued): **Early AO journal publications.** Either rated as essential by J. Prein, or mentioned as core paper by current AO employees. Ordered by year of publication; ° Source: Web of Science.

10.4.3 AO Core papers appearing in journals with high Impact Factors

IF°	Journal	Year of publ. (IF*)	Authors	Title	Dept/ Divis.	Total Citations°
24.01	J clin oncol	2016	Fehlings MG, Nater A, Tetreault L, Kopjar B, Arnold P, Dekutoski M, Finkelstein J, Fisher C, France J, Gokaslan Z, Massicotte E, Rhines L, Rose P, Sahgal A, Schuster J, Vaccaro A.	Survival and clinical outcomes in surgically treated patients with metastatic epidural spinal cord compression: results of the prospective multicenter AOSpine study.	Spine	16
10.02	Nat commun	2012	Sakai D, Nakamura Y, Nakai T, Mishima T, Kato S, Grad S, Alini M, Risbud MV, Chan D, Cheah KS, Yamamura K, Masuda K, Okano H, Ando K, Mochida J.	Exhaustion of nucleus pulposus progenitor cells with ageing and degeneration of the intervertebral disc.	ARI/Spine	807
9.92	Brain	2012	Granger N, Blamires H, Franklin RJ, Jeffery ND.	Autologous olfactory mucosal cell transplants in clinical spinal cord injury: a randomized double-blinded trial in a canine translational model.	VET	354
9.81	Arch Intern Med	2009	Friedman SM, Mendelson DA, Bingham KW, Kates SL.	Impact of a comanaged geriatric fracture center on short-term Hip Fracture Outcomes	CID	1'549
9.68	Proc natl Acad Sci USA	2011	Bowles RD, Gebhard HH, Härtl R, Bonassar LJ.	Tissue-engineered intervertebral discs produce new matrix, maintain disc height, and restore biomechanical function to the rodent spine.	Spine	753

Table A6.2: **List of publications with Impact Factors (IF) above the limits set.** Ordered by IF; ° Source: Web of Science; * year of IF, if IF in the year of publication was not available.

IF°	Journal	Year of publ. (IF*)	Authors	Title	Dept/ Divis.	Total Ci-tations°
9.67	J clin invest	1996 (1997)	Antoniou J, Steffen T, Nelson F, Winterbottom N, Hollander AP, Poole AR, Aebi M, Alini M.	The human lumbar intervertebral disc: evidence for changes in the biosynthesis and denaturation of the extracellular matrix with growth, maturation, ageing and degeneration	ARI	16'876
9.65	Eur Cell Mat	2010	Verrier S, Meury T, Kupcsik L, Heini P, Stool T, Alini M.	Platelet-released supernatant induces osteoblastic differentiation of human mesenchymal stem cells via BPM-2 up-regulation: potential use for autologous growth factors source.	ARI	339
8.56	Biomaterials	2014	Inzana J, Olvera D, Fuller S, Kelly J, Graeve O, Schwarz E, Kates S, Awad H.	3D printing of composite calcium phosphate and collagen scaffolds for bone regeneration.	ARI /Trauma CPP BI	930
8.39	Biomaterials	2015	Pirvu T, Blanquer S, Benneker L, Grijpma D, Richards RG, Alini M, Eglin D, Grad S, Li Z.	A combined biomaterial and cellular approach for annulus fibrosus rupture repair.	ARI	102
6.44	J bone Miner Res	2008	Sample SJ, Behan M, Smith L, Oldenhoff WE, Markel MD, Kalscheur VL, Hao Z, Miletic V, Muir P.	Functional adaptation to loading of a single bone is neuronally regulated and involves multiple bones.	VET	872
6.32	Acta Biomater	2017 (2016)	Guillaume O, Geven MA, Sprecher CM, Stadelmann VA, Grijpma DW, Tang TT, Qin L, Lai Y, Alini M, de Bruijn JD, Yuan H, Richards RG, Eglin D.	Surface-enrichment with hydroxyapatite nanoparticles in stereolithography-fabricated composite polymer scaffolds promotes bone repair.	ARI	n.a.

Table A6.2 (continued): **List of publications with Impact Factors (IF) above the limits set.** Ordered by IF; ° Source: Web of Science; * year of IF, if IF in the year of publication was not available.

IF°	Journal	Year of publ. (IF*)	Authors	Title	Dept/ Divis.	Total Ci-tations°
6.32	Acta Biomater	2016	ter Boo GA, Arens D, Metsemakers WJ, Zeiter S, Richards RG, Grijpma DW, Eglin D, Moriarty TF.	Injectable gentamicin-loaded thermo-responsive hyaluronic acid derivative prevents infection in a rabbit model.	ARI	0
6.32	Acta Biomater	2016	Yang Y, Yang S, Wang Y, Yu Z, Ao H, Zhang H, Qin L, Guillaume O, Eglin D, Richards RG, Tang T.	Anti-infective efficacy, cytocompatibility and bio-compatibility of a 3D-printed osteoconductive composite scaffold functionalized with quater-nized chitosan.	ARI	0
6.28	J bone Miner Res	2016	Bentley KLD, Trombetta R, Nishitani K, Bello-Irizarry S, Ninomiya M, Zhang L, Chung H, Mcgrath J, Daiss J, Awad H, Kates S, Schwarz EM.	Evidence of Staphylococcus aureus deformation, proliferation and migration in canaliculi of live cortical bone in murine models of osteomyelitis.	Trauma CPP BI	0
5.33	Biomacromlecules	2010	Mortisen S, Peroglio M, Alini M, Eglin D.	Tailoring thermoreversible hyaluronan hydrogels by “click” chemistry and RAFT polymerization for cell and drug therapy.	ARI	1'602
5.28	J Bone Joint Surg Am	2014	Kralinger F, Blauth M, Goldhahn J, Käch K, Voigt C, Platz A, Hanson B.	The influence of local bone density on the out-come of one hundred and fifty proximal humeral fractures treated with a locking plate.	Trauma CPP FFOB	17
5.23	Sci Rep	2015	Kazezian Z, Gawri R, Haglund L, Ouellet J, Mwale F, Tarrant F, O'Gaora P, Pandit A, Alini M, Grad S.	Gene expression profiling identifies interferon sig-nalling molecules and IGFBP3 in human degenera-tive annulus fibrosus.	ARI	3

Table A6.2 (continued): **List of publications with Impact Factors (IF) above the limits set.** Ordered by IF; ° Source: Web of Science; * year of IF, if IF in the year of publication was not available.

IF°	Journal	Year of publ. (IF*)	Authors	Title	Dept/ Divis.	Total Ci-tations°
4.89	Eur Cell Mat	2013	Johnstone B, Alini M, Cucchiarini M, Dodge GR, Eglin D, Guilak F, Madry H, Mata A, Mauck RL, Semino CE, Stoddart MJ.	Tissue engineering for articular cartilage repair--the state of the art.	ARI	905
4.89	Eur Cell Mat	2013	Gawri R, Antoniou J, Ouellet J, Awwad W, Steffen T, Roughley P, Haglund L, Mwale F.	Link-N can stimulate proteoglycan synthesis in the degenerated human intervertebral discs.	Spine	263
4.89	Eur Cell Mat	2014	Bruderer M, Richards RG, Alini M, Stoddart MJ.	Role and regulation of RUNX2 in osteogenesis.	ARI	177
4.89	Eur Cell Mat	2014	Czekanska EM, Ralphs JR, Alini M, Stoddart MJ.	Enhancing inflammatory and chemotactic signals to regulate bone regeneration.	ARI	25
4.89	Eur Cell Mat	2014	Pattappa G, Peroglio M, Sakai D, Mochida J, Benneker LM, Alini M, Grad S.	CCL5/RANTES is a key chemoattractant released by degenerative intervertebral discs in organ culture.	ARI	335
4.89	Eur Cell Mat	2014	Reizner W, Hunter J, O'Malley N, Southgate R, Schwarz E, Kates S.	A systematic review of animal models for Staphylococcus aureus osteomyelitis.	Trauma CPP BI	76
4.86	Osteoporos int	2010	Kammerlander C, Roth T, Friedman SM, Suhm N, Luger TJ, Kammerlander-Knauer U, Krappinger D, Blauth M.	Ortho-geriatric service-a literature review comparing different models.	Trauma CPP FFOB	937
4.84	J Bone Joint Surg Am	2016	Wagner D, Kamer L, Sawaguchi T, Richards RG, Noser H, Rommens PM.	Sacral bone mass distribution assessed by averaged three-dimensional CT models: implications for pathogenesis and treatment of fragility fractures of the sacrum.	ARI	1

Table A6.2(continued): **List of publications with Impact Factors (IF) above the limits set.** Ordered by IF; ° Source: Web of Science; * year of IF, if IF in the year of publication was not available.

IF°	Journal	Year of publ. (IF*)	Authors	Title	Dept/ Divis.	Total Ci-tations°
4.82	J cell molec med	2010	Li Z, Kupcsik L, Alini M, Yao SJ, Stoddart M.	Mechanical load modulates chondrogenesis of human mesenchymal stem cells through the TGF-beta pathway.	ARI	1'662
4.56	Eur Cell Mat	2015	Arens D, Wilke M, Calabro L, Hackl S, Zeiter S, Zderic I, Richards RG, Moriarty TF.	A rabbit humerus model of plating and nailing osteosynthesis with and without staphylococcus aureus osteomyelitis.	ARI	5
4.56	Eur Cell Mat	2015	Inzana J, Kates S, Trombetta R, Schwarz E, Awad H.	3D printed bioceramics for dual antibiotic delivery to treat implant-associated bone infection	Trauma CPP BI	59
4.45	Tissue Eng Part A	2014	Loebel C, Czekanska EM, Bruderer M, Salzmann G, Alini M, Stoddart MJ.	In vitro osteogenic potential of human mesenchymal stem cells is predicted by Runx2/Sox9 ratio	ARI	113
4.31	J Bone Joint Surg Am	2013	Gedbjerg N, LaRosa R, Hunter JG, Varrone JJ, Kates SL, Schwarz E, Daiss JL.	Anti-glucosaminidase IgG in sera as a biomarker of host immunity against staphylococcus aureus in orthopaedic surgery patients	Trauma CPP BI	25
4.29	Osteoporos int	2008	Goldhahn J, Suhm N, Goldhahn S, Blauth M, Hanson B.	Influence of osteoporosis on fracture fixation--a systematic literature review.	Trauma CPP FFOB	515
4.26	Sci Rep	2016	Li B, Menzel U, Loebel C, Schmal H, Alini M, Stoddart MJ.	Monitoring live human mesenchymal stromal cell differentiation and subsequent selection using fluorescent RNA-based probes.	ARI	1
4.02	Bone	2011	Wirth AJ, Goldhahn J, Flaig C, Arbenz P, Müller R, van Lenthe GH.	Implant stability is affected by local bone microstructural quality.	Trauma CPP FFOB	155

Table A6.2 (continued): **List of publications with Impact Factors (IF) above the limits set.** Ordered by IF; ° Source: Web of Science; * year of IF, if IF in the year of publication was not available.

IF°	Journal	Year of publ. (IF*)	Authors	Title	Dept/ Divis.	Total Ci-tations°
4.00	Eur Cell Mat	2016	Grad S, Bow C, Karppinen J, Luk KD, Cheung KM, Alini M, Samartzis D.	Systemic blood plasma CCL5 and CXCL6: Potential biomarkers for human lumbar disc degeneration.	ARI	4
4.00	Eur Cell Mat	2016	Gardner OF, Fahy N, Alini M, Stoddart MJ	Differences in human mesenchymal stem cell secretomes during chondrogenic. induction.	ARI	2
4.00	Eur Cell Mat	2016	Hulsart-Billstrom G, Dawson JI, Hofmann S, Muller R, Stoddart MJ, Alini M, Redl H, El Haj A, Brown R, Salih V, Hilborn J, Larsson S, Oreffo RO.	A surprisingly poor correlation between in vivo and in vivo testing of biomaterials for bone regeneration: results of a multicentre analysis.	ARI	1
4.00	Eur Cell Mat	2017 (2016)	Moriarty TF, Schmid T, Post V, Samara E, Kates S, Schwarz EM, Zeiter S, Richards RG.	A large animal model for a failed two-stage revision of intramedullary nail-related infection by methicillin-resistant Staphylococcus aureus.	ARI / Trauma CPP BI	n.a.
4.00	Bone	2000	Johnson KA, Muir P, Nicoll RG, Roush JK.	Asymmetric adaptive modeling of central tarsal bones in racing greyhounds.	VET	1'509
3.73	PLoS One	2012	Fehlings MG, Vaccaro A, Wilson JR, Singh A, W Cadotte D, Harrop JS, Aarabi B, Shaffrey C, Dvorak M, Fisher C, Arnold P, Massicotte EM, Lewis S, Rampersaud R.	Early versus delayed decompression for traumatic cervical spinal cord injury: results of the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS).	CID	1'470
3.43	J Bone Joint Surg Am	2009	Konrad G, Bayer J, Hepp P, Voigt C, Oestern H, Kääb M, Luo C, Plecko M, Wendt K, Köstler W, Südkamp N.	Open reduction and internal fixation of proximal humeral fractures with use of the locking proximal humerus plate. Surgical technique.	CID	1'851

Table A6.2 (continued): **List of publications with Impact Factors (IF) above the limits set.** Ordered by IF; ° Source: Web of Science; * year of IF, if IF in the year of publication was not available.

IF°	Journal	Year of publ. (IF*)	Authors	Title	Dept/ Divis.	Total Ci-tations°
2.29	Equine Vet J	2012	Carlson ER, Bramlage LR, Stewart AA, Embertson RM, Ruggles AJ, Hopper SA.	Complications after two transphyseal bridging techniques for treatment of angular limb deformities of the distal radius in 568 thoroughbred yearlings.	VET	2

Table A6.2 (continued): **List of publications with Impact Factors (IF) above the limits set.** Ordered by IF; ° Source: Web of Science; * year of IF, if IF in the year of publication was not available.

10.4.4 Citation trends of early book and journal publications in detail

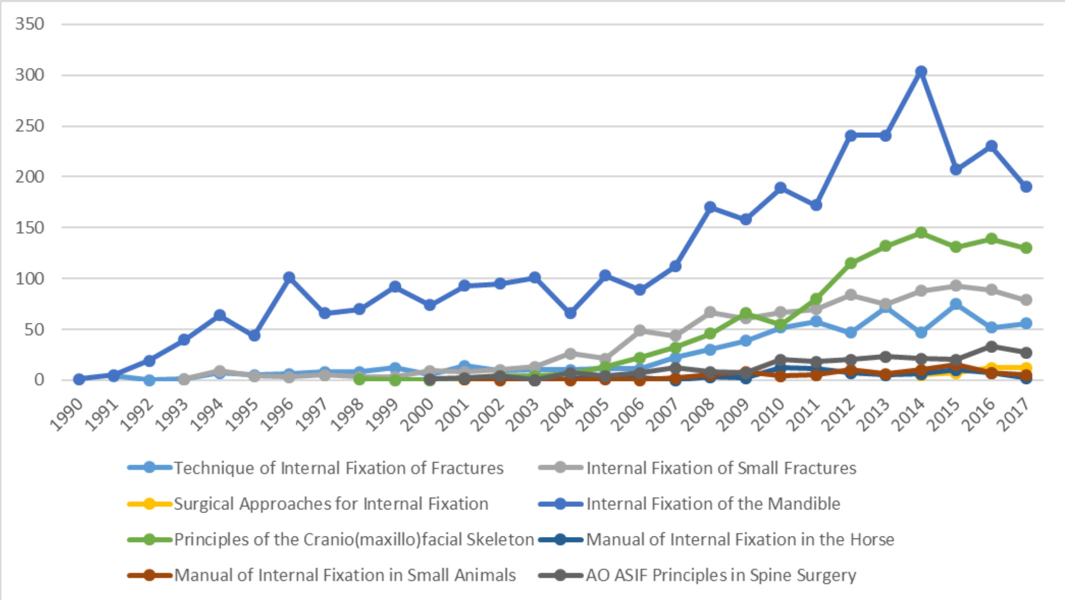

Figure A6.1: **Citation trends 1990-2017 of AO core books without the three most cited books**. Source: Web of Science; all editions considered; last update: 30.11.2017

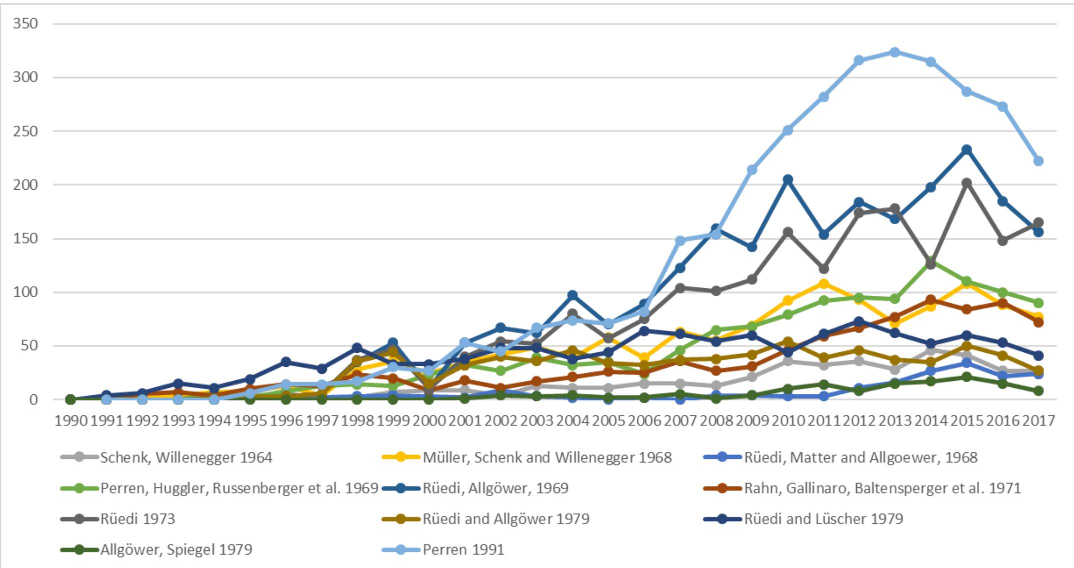

Figure A6.2: **Citation trends 1990-2017 of early AO core papers published between 1959 and 2005 without the two most cited papers**. Ordered by publication year. Source: Web of Science; last update: 23.11.2017

10.4.5 InCites highly cited thresholds from

Explanations to highly cited thresholds from the Clarivate Analytics (https://esi.incites.thomsonreuters.com/ThresholdsAction.action, last update: 11.12.2017):

“Highly Cited Thresholds:

The highly cited threshold is the minimum number of citations received by the top 1% of papers in the research field published in the specified year.

When the threshold is calculated to be 2 or fewer for a subject category in a given year, no paper in that category and year receives a Highly Cited designation. This low threshold decision is based on observations that only two citations is small evidence of highly cited paper status. Papers cited at low levels tend to exhibit more volatility with respect to highly cited status over subsequent ESI updates.

Sample Report:

In the following report, the top 1% of papers in Physics added to Web of Science in 2010 received at least 44 citations. The top 1% of papers in Plant & Animal Science added to Web of Science in 2011 received at least 16 citations. Articles citing the 2010 papers may have been published between 2010 and 2013. Articles citing the 2011 papers may have been published between 2011 and 2013.”

FIELD	2009	2010	2011	2012	2013
PHYSICS	61	44	26	10	0
PLANT & ANIMAL SCIENCE	42	29	16	6	0

RESEARCH FIELDS	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
AGRICULTURAL SCIENCES	132	114	94	92	71	60	47	35	22	11	3
BIOLOGY & BIOCHEMISTRY	257	234	212	180	147	120	95	68	42	18	5
CHEMISTRY	199	195	180	173	161	135	108	83	53	24	6
CLINICAL MEDICINE	218	196	176	154	129	106	82	60	39	18	5
COMPUTER SCIENCE	108	104	88	84	72	58	50	40	25	12	4
ECONOMICS & BUSINESS	179	145	121	110	84	63	46	30	18	8	3
ENGINEERING	113	101	99	90	76	62	50	38	25	13	4
ENVIRONMENT/ECOLOGY	224	206	178	156	127	108	79	55	34	15	4
GEOSCIENCES	178	170	155	127	115	92	73	49	30	14	5
IMMUNOLOGY	329	293	266	224	181	149	120	87	52	24	6
MATERIALS SCIENCE	193	173	173	168	148	128	100	78	50	23	5
MATHEMATICS	77	69	60	57	44	35	26	20	13	7	3
MICROBIOLOGY	208	207	193	170	126	114	88	60	40	20	4
MOLECULAR BIOLOGY & GENETICS	507	440	389	337	283	224	169	117	69	29	6
MULTIDISCIPLINARY	525	391	388	444	245	156	150	92	65	21	4
NEUROSCIENCE & BEHAVIOR	285	252	224	196	154	127	97	68	41	19	5
PHARMACOLOGY & TOXICOLOGY	191	184	154	130	108	90	70	52	31	14	4
PHYSICS	169	169	152	143	120	106	84	65	42	21	5
PLANT & ANIMAL SCIENCE	148	126	117	104	84	68	52	39	24	12	4
PSYCHIATRY/PSYCHOLOGY	229	194	167	149	117	86	65	45	26	12	4
SOCIAL SCIENCES, GENERAL	129	109	92	83	65	52	40	29	17	8	4
SPACE SCIENCE	246	218	213	182	160	137	118	80	55	29	7

Figure A6.3: **Highly cited thresholds 2007 – 2017.** Source: https://esi.incites.thomson-reuters.com/ThresholdsAction.action. Last update: 11.12.2017

10.4.6 InCites hot paper thresholds

Explanations to hot paper thresholds from the Clarivate Analytics (https://esi.incites.thomsonreuters.com/ThresholdsAction.action, last update 11.12.2017):

«Hot Paper Thresholds:

Hot papers are papers that receive a large number of citations soon after publication, relative to other papers of the same field and age. More precisely, they are papers published in the past two years that received a number of citations in the most recent two-month period that places them in the top 0.1% of papers in the same field.

Time period for counts:

We measure age for hot papers in two-month periods rather than years, and we scan only those papers published in the last two years to see if they are receiving more citations than the norm. To get a very current sampling of citations, we count citations from only the most recent two-month period. The time periods are defined by database processing dates (the actual date when items are entered into the database, which is not necessarily the publication date). Note that the data is updated bimonthly (six times a year).

Field and age variations: To correct for field variations in citation rate, each field is treated separately. Furthermore, since older papers tend to be cited more than newer (just published) papers, a separate analysis is made for each two-month grouping of papers, giving a total of 12 groupings over the two-year period.

Sample Report:

The following excerpt shows ten two-month periods, beginning with the fourth period (July-August) of 2011. The most recent two-month period is 2013-1 (January-February 2013). This report reveals that a paper in the field of Chemistry is "hot" if:

- It was added to Web of Science in the 4th period of 2011, and it received at least 14 citations in the most recent two-month period.
- It was added to Web of Science in the 2nd period of 2012, and it received at least 12 citations in the most recent two-month period.
- It was added to Web of Science in the 1st period of 2013, and it received at least 3 citations in the most recent two-month period.

FIELD	**2011-4**	**2011-5**	**2011-6**	**2012-1**	**2012-2**	**2012-3**	**2012-4**	**2012-5**	**2012-6**	**2013-1**
CHEMISTRY	14	11	12	11	12	9	8	6	4	3

When the header of the last column changes to 2013-2, different numbers can appear in some or all of the columns. Those numbers may be larger or smaller because only citation data from the current two-month period is used to generate the counts in all of the columns.

Be aware that the *total* number of citations received by a hot paper will likely be higher than the number shown in any one of these columns--which is only the number of citations received in the current two-month period."

RESEARCH FIELDS	2015-5	2015-6	2016-1	2016-2	2016-3	2016-4	2016-5	2016-6	2017-1	2017-2	2017-3	2017-4
AGRICULTURAL SCIENCES	6	6	5	5	5	5	5	5	4	3	3	3
BIOLOGY & BIOCHEMISTRY	12	12	14	12	9	14	8	7	7	6	4	4
CHEMISTRY	16	15	15	17	12	12	14	11	9	7	5	4
CLINICAL MEDICINE	14	12	11	13	11	12	11	9	7	6	4	4
COMPUTER SCIENCE	8	7	10	11	6	7	6	7	6	5	4	4
ECONOMICS & BUSINESS	5	5	4	4	4	5	3	4	3	2	2	5
ENGINEERING	8	6	7	7	7	7	7	5	5	4	4	3
ENVIRONMENT/ECOLOGY	10	7	7	7	9	7	7	6	5	4	3	5
GEOSCIENCES	9	8	8	7	7	7	6	6	5	4	4	8
IMMUNOLOGY	12	12	12	14	13	14	15	8	8	6	5	3
MATERIALS SCIENCE	14	12	12	14	16	12	11	10	9	6	5	3
MATHEMATICS	6	4	4	4	4	4	4	4	3	3	3	3
MICROBIOLOGY	11	12	10	10	16	15	11	11	6	8	5	3
MOLECULAR BIOLOGY & GENETICS	19	19	16	15	18	15	13	12	9	7	6	3
MULTIDISCIPLINARY	14	49	12	10	15	7	10	14	9	4	3	5
NEUROSCIENCE & BEHAVIOR	13	10	11	12	10	10	8	7	6	5	4	4
PHARMACOLOGY & TOXICOLOGY	7	10	6	7	7	7	7	6	6	5	4	4
PHYSICS	13	10	11	10	16	11	11	10	8	7	6	5
PLANT & ANIMAL SCIENCE	6	6	6	6	7	5	5	5	4	4	3	5
PSYCHIATRY/PSYCHOLOGY	6	7	6	8	7	6	5	5	4	4	3	6
SOCIAL SCIENCES, GENERAL	5	5	5	5	5	4	4	4	3	3	3	7
SPACE SCIENCE	11	10	13	15	12	20	26	18	14	8	6	6

Figure A6.4: **Hot paper thresholds May 2015 – April 2017.** Source: https://esi.incites.thomsonreuters.com/ThresholdsAction.action. Last update: 11.12.2017

10.4.7 Publications in journals with high impact factors

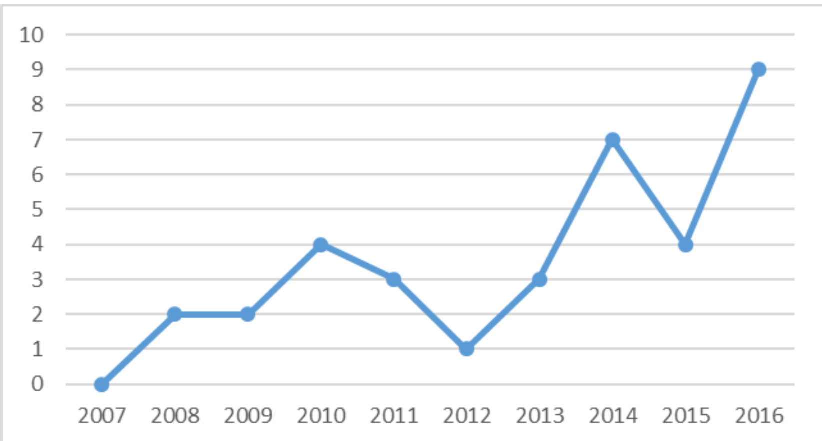

Figure A6.5: **Number of AO publications in journals with impact factors (IF) over 4.0 (2008 – 2016)**. Source: Web of Science; last update: 22.11.2017

10.4.8 Citation trends by departments / divisions

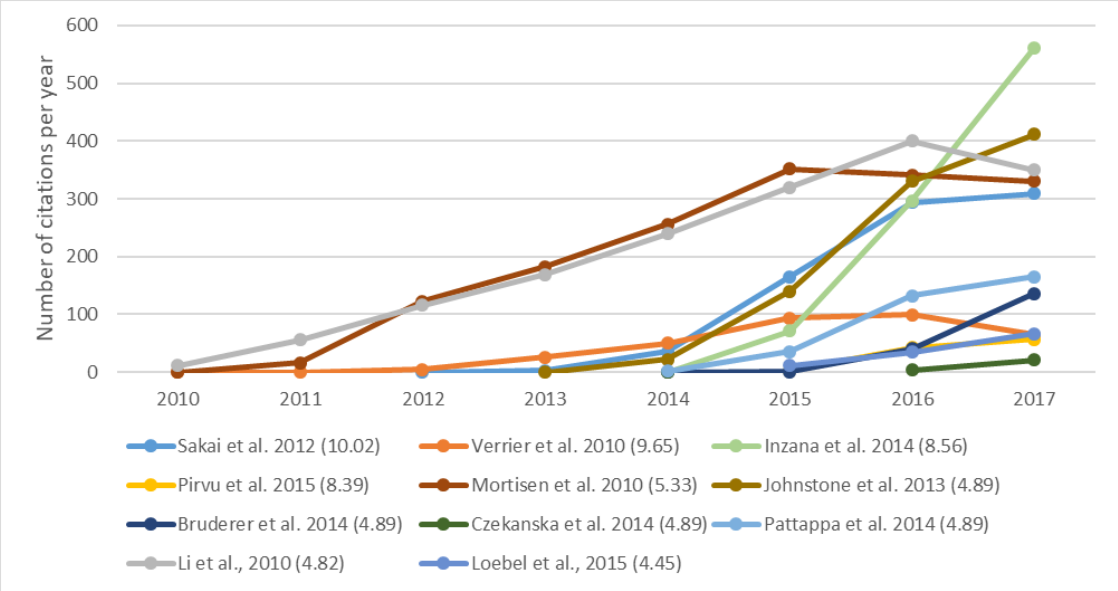

Figure A6.6: **Citation trends of the most influential ARI journal publications**. Source: Web of Science; Impact Factor in brackets; last update: 22.11.2017

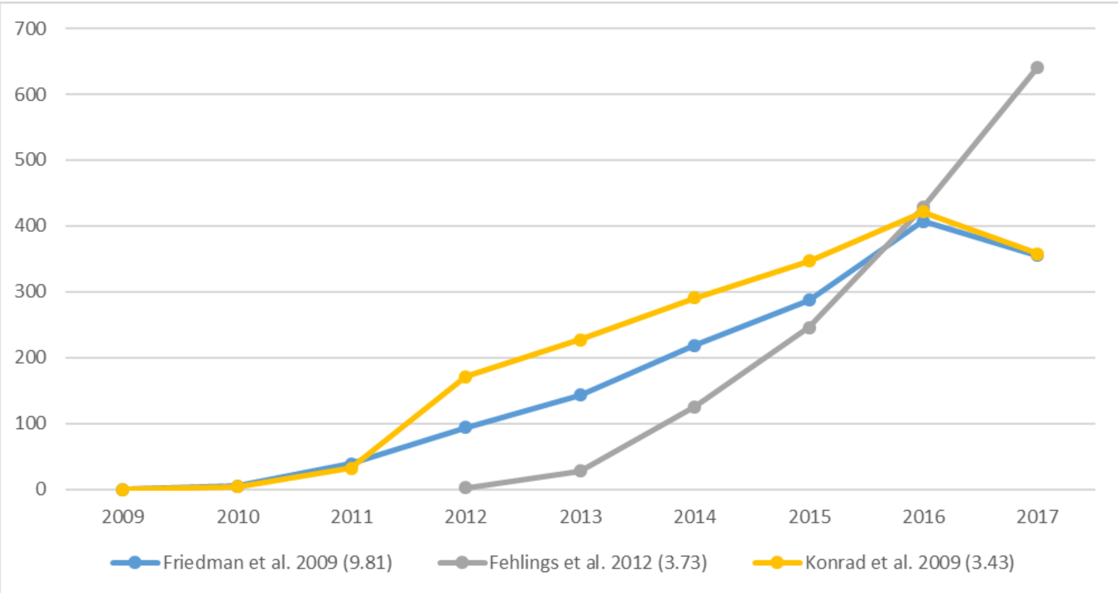

Figure A6.7: **Citation trends of the most influential CID journal publications**. Source: Web of Science; Impact Factor in brackets; last update: 27.11.2017

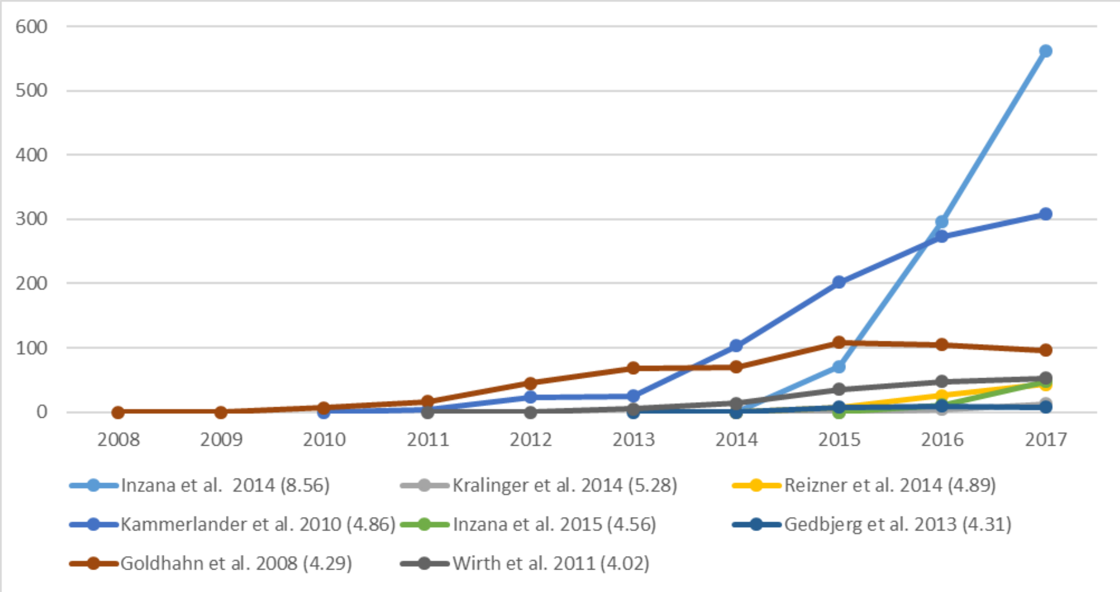

Figure A6.8: **Citation trends of the most influential AOTrauma journal publications**. Source: Web of Science; contains publications from two AO clinical priority programs (CPP): Bone infection and Osteoporotic bone; Impact Factor in brackets; last update: 22.11.2017

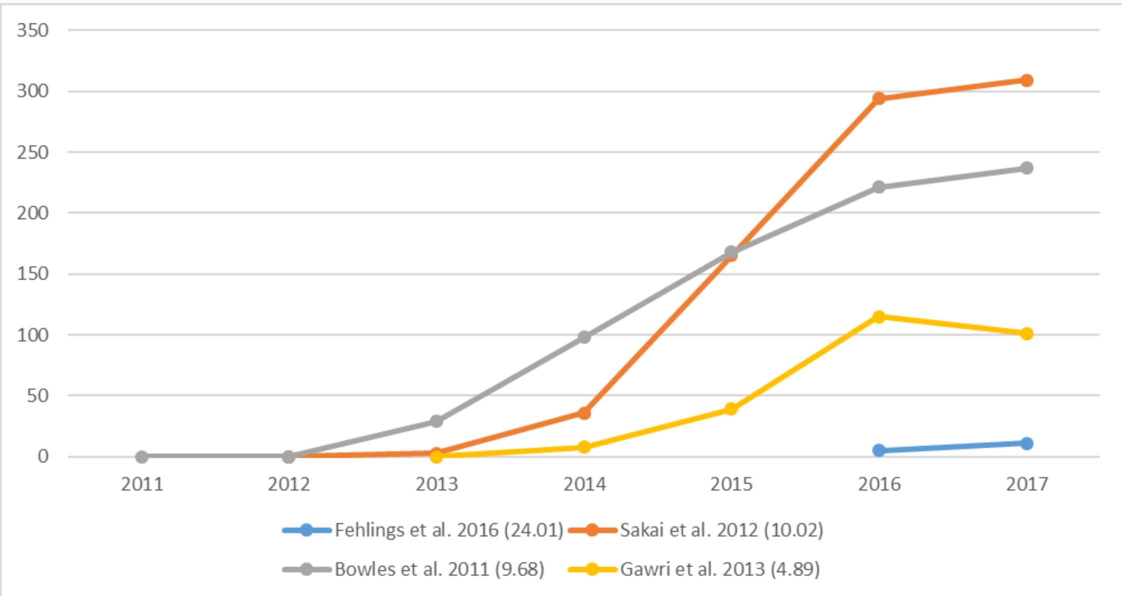

Figure A6.9: **Citation trends of most influential Spine journal publications**. Source: Web of Science; Impact Factor in brackets; last update: 22.11.2017

The CMF division preferred to mention the top five contributions from the AO that have changed the way surgeons work today, instead of providing a list of publications from their field. Their aim was to avoid discrimination of surgeons who did not appear on these first publications but did a great amount of work in the same field. Therefore, only the five most important topics in CMF will be listed in this report:

1) Improvements of surgical approach to the facial skeleton (move to the open treatment of facial fractures)
2) Stable internal fixation that includes locking plate/screw systems/THORP (Titanium Hollow Screw Osseous Integrating Re-construction Plate)
3) Computer-Assisted Surgery (includes virtual surgical planning, navigation, use of models, patient-specific implants, cutting/drill guides)
4) Microvascular reconstruction in the CMF region
5) Peri- and intra-Operation imaging like medical CT/CBCT (Computer Tomography/Cone Beam Computer Tomography)

Exponents of AO CMF were not certain, whether the last two topics were related to AO activities.

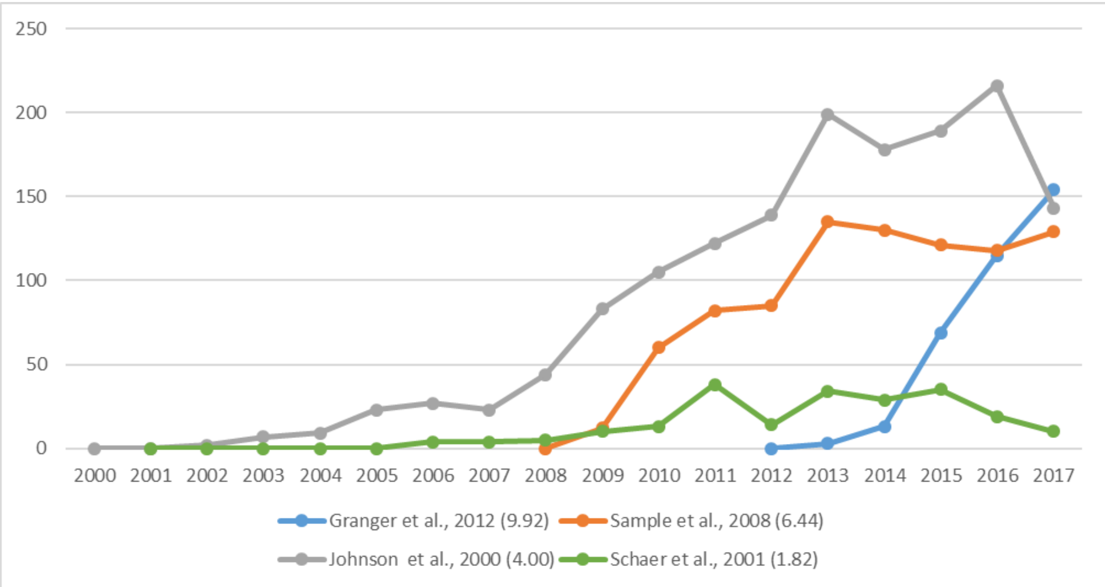

Figure A6.10: **Citation trends of most influential VET journal publications**. Source: Web of Science; Impact Factor in brackets; last update: 22.11.2017

10.4.9 Involvement of ARI employees in boards of scientific or medical associations

The following list is a very incomplete collection of persons of the AO Foundation involved in boards of scientific or medical associations, as we only received data from ARI and AOVET. Nevertheless, we report this data in the Appendix to give a rough impression of the variety of involvements of AO employees in boards of scientific or medical associations. Other persons, for example from AOT, AOS and AOCMF and not part of this list, do also contribute to disseminate knowledge and scientific competence via engagement as a board member.

Mauro Alini: Board of Directors and Membership Committee Orthopaedic Research Society (ORS); Steering Committee International Combined Orthopaedic Research Societies (ICORS); Council Member of Tissue Engineering and Regenerative Medicine International Society European Chapter (TERMIS-EU); Education and Meeting Committee International Cartilage Repair Society (ICRS); President Swiss Bone Mineral Society (SBMS)

David Eglin: Secretary Executive Committee Swiss Society for Biomaterials and Regenerative Medicine (SSB&RM); Committee Member of TERMIS-EU European Chapter Meeting

Sybille Grad: Editorial Board Member of European Cells & Materials Journal International; Editorial Board Member of Scoliosis & Spinal Disorders Journal International; Advisory Review Board Member of Journal of Orthopaedic Research Spine; Spine Section Research Chair, Program Committee Member and Spine Research Interest Group co-organizer ORS; Annual conference co-organiser of European Cells & Materials; Committee Member of TERMIS-EU European Chapter Meeting; Annual Meeting Committee Member of BioSpine; Fellow Member of International Cartilage Repair Society (ICRS)

Geoff Richards: Chair of the International College of Fellows for Orthopaedic Research (nominated and approved by the ICORS board which governs International College); Steering Committee ICORS; International Advisory Committee for annual meetings European Society for Biomaterials (ESB); Executive Committee member European Orthopaedic Research Society (EORS); Chair of the Infection Committee ORS; Associate Editor Journal of Orthopaedic Translation; Editor-in-Chief, webmaster, webeditor eCM journal

Martin Stoddart: Chair of Basic Science Education committee and Member of Communications Council ORS; Deputy Co-Chair Basic Science committee ICRS

Sophie Verrier: Board Member Swiss Bone and Mineral Society (SBMS); Co-chair Women's Leadership Forum and Member Anual Meeting Committee ORS

Stephan Zeitner: Chair elect Preclinical Model Section ORS; Member of the council and education committee European College of Laboratory Animal Medicine (ECLAM); Member of the scientific committee of the Swiss Laboratory Animals Science Association (SGV)

10.4.10 Involvement of AOVET members in boards of scientific or veterinary associations

The following list is a very incomplete collection of persons of the AO Foundation involved in boards of scientific or medical associations, as we only received data from ARI and AOVET. Nevertheless, we report this data in the Appendix to give a rough impression of the variety of involvements of AO employees in boards of scientific or medical associations. Other persons, for example from AOT, AOS and AOCMF and not part of this list, do also contribute to disseminate knowledge and scientific competence via engagement as a board member.

Professor Jörg Auer: Chairman Examination Committee of the American College of Veterinary Surgeons (ACVS); President of Veterinary Orthopedic Society; President of the European College of Veterinary Surgeons (ECVS); Vice President of the Foundation Research for Horses, Switzerland; President of the Foundation Research for Horses

Professor Larry Bramlage: President-elect of the ACVS; President of the American Association of Equine Practioners; Board of Directors of the Grayson-Jockey Club Research Foundation; Review Board of Equine Veterinary Journal

Dr Wade O Brinker: Founding diplomate and President of the ACVS

Dr John Houlton: Diplomate and Executive Secretary of the ECVS

Professor Kenneth A Johnson: Editor in Chief of the Veterinary and Comparative Orthopaedics Journal

Professor Uli Matis: President of the ECVS; European Society of Veterinary Orthopaedics and Traumatology (ESVOT) meeting in Munich

Dr Donald Piermattei: President of the ACVS; President of the Veterinary Orthopedic Society (VOS), Editor of the Veterinary Surgery Journal

Professor Geoff Sumner Smith: Founding Member of the British Veterinary Orthopaedic Association (BVOA); Founding Editor in Chief of the Veterinary and Comparative Orthopaedics Journal