

The history of the discovery of the cigarette—lung cancer link: evidentiary traditions, corporate denial, global toll

Robert N Proctor

Correspondence to

Dr Robert N Proctor, History Department, Stanford University, Stanford, California 94305, USA; rproctor@stanford.edu

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ABSTRACT

Lung cancer was once a very rare disease, so rare that doctors took special notice when confronted with a case, thinking it a once-in-a-lifetime oddity. Mechanisation and mass marketing towards the end of the 19th century popularised the cigarette habit, however, causing a global lung cancer epidemic. Cigarettes were recognised as the cause of the epidemic in the 1940s and 1950s, with the confluence of studies from epidemiology, animal experiments, cellular pathology and chemical analytics. Cigarette manufacturers disputed this evidence, as part of an orchestrated conspiracy to salvage cigarette sales. Propagandising the public proved successful, judging from secret tobacco industry measurements of the impact of denialist propaganda. As late as 1960 only one-third of all US doctors believed that the case against cigarettes had been established. The cigarette is the deadliest artefact in the history of human civilisation. Cigarettes cause about 1 lung cancer death per 3 or 4 million smoked, which explains why the scale of the epidemic is so large today. Cigarettes cause about 1.5 million deaths from lung cancer per year, a number that will rise to nearly 2 million per year by the 2020s or 2030s, even if consumption rates decline in the interim. Part of the ease of cigarette manufacturing stems from the ubiquity of high-speed cigarette making machines, which crank out 20 000 cigarettes per min. Cigarette makers make about a penny in profit for every cigarette sold, which means that the value of a life to a cigarette maker is about US\$10 000.

Lung cancer has become a formidable disease, killing about 1.5 million people per year globally, extrapolating from a 2008 International Agency for Research on Cancer (IARC) risk assessment.¹ The tragedy is magnified by the fact that the overwhelming majority of these deaths, around 95%, are entirely preventable. Lung cancer today is primarily caused by the inhalation of smoke from cigarettes, which is also why the disease was quite rare prior to the 20th century. Lung cancer was not even recognised medically until the 18th century, and as recently as 1900 only about 140 cases were known in the published medical literature. The malady must have been occasionally misdiagnosed as tuberculosis (phthisis) or pneumonia or some other lung malaise, but we also know from detailed autopsy records in Germany that the disease cannot have been very common. Findings of primary lung tumours in the autopsied bodies of German research clinics rose dramatically in the second half of the 19th century, and even more dramatically in the first decade of the 20th. Isaac

Adler summarised this evidence in 1912, in the world's first monograph on lung cancer, noting that the incidence of malignant neoplasms of the lung seemed to show 'a decided increase'. Adler mentioned the 'abuse of tobacco and alcohol' as one possible cause, while also commenting that the subject was 'not yet ready for final judgment'.²

Tobacco was apparently not even suspected as a cause of lung tumours until the final decade of the 19th century. In 1898, a medical student by the name of Hermann Rottmann in Würzburg proposed that tobacco dust—not smoke—might be causing the elevated incidence of lung tumours among German tobacco workers. Rottmann's mistake was not corrected until 1912, when Adler proposed that smoking might be to blame for the growing incidence of pulmonary tumours. Lung cancer was still a very rare disease; so rare, in fact, that medical professors when confronted with a case sometimes told their students they might never see another.³ By the 1920s, however, surgeons were encountering the malady with increasing frequency, and started puzzling over what might be responsible. Smoking was commonly blamed, along with asphalt dust from newly tarred roads, industrial air pollution and latent effects from exposure to poison gas in the First World War or the global influenza pandemic of 1918–1919. These and a number of other theories were put forward as possible explanations for the rise of lung cancer, until evidence from multiple sources of enquiry made it clear that tobacco was by far and away the leading culprit.

CONVERGING LINES OF EVIDENCE

In the middle decades of the 20th century, four distinct lines of evidence converged to establish cigarette smoking as the leading cause of lung cancer. These are outlined below.

Population studies

These were among the first and most convincing forms of evidence. Scholars started noting the parallel rise in cigarette consumption and lung cancer, and by the 1930s had begun to investigate this relationship using the methods of case-control epidemiology. Franz Hermann Müller at Cologne Hospital in 1939 published the first such study, comparing 86 lung cancer 'cases' and a similar number of cancer-free controls.⁴ Müller was able to show that people with lung cancer were far more likely than non-cancer controls to have smoked, a fact confirmed by Eberhard Schairer and Eric Schöniger at the University of Jena in an even more

ambitious study from 1943.⁵ These German results were subsequently verified and amplified by UK and American scholars: in 1950 alone, five separate epidemiological studies were published, including papers by Ernst Wynder and Evarts Graham in the USA and Richard Doll and A Bradford Hill in England. All confirmed this growing suspicion, that smokers of cigarettes were far more likely to contract lung cancer than non-smokers. Further confirmation came shortly thereafter from a series of prospective 'cohort' studies, conducted to eliminate the possibility of recall bias. The theory here was that by following two separate and initially healthy groups over time, one smoking and one non-smoking, matched by age, sex, occupation and other relevant traits, you could find out whether smoking was a factor in the genesis of lung disease. The results were unequivocal: Doll and Hill in 1954 concluded that smokers of 35 or more cigarettes per day increased their odds of dying from lung cancer by a factor of 40.⁶ Hammond and Horn, working with the American Cancer Society on another large cohort study, concluded that same year that the link had been proven 'beyond a reasonable doubt'.^{7 8}

Animal experimentation

This was a second key line of evidence. 'Tobacco juice' had been shown to cause cancer on laboratory animals since the first decade of the century,⁹ and a number of scholars had confirmed these results. The most active in this realm was the intrepid Angel H Roffo, founding director of Argentina's Institute of Experimental Medicine for the Study and Treatment of Cancer, who in 1931 showed that smoke condensed from the destructive distillation of tobacco could cause tumours when smeared on the hairless skins of rabbits.¹⁰ Roffo in the 1930s and early 1940s published dozens of articles (mainly in German and Spanish) implicating smoking in the genesis of cancer, prompting enthusiastic endorsement from the German public health establishment but also ridicule from the cigarette industry. German tobacco manufacturers even established an entire journal—*Chronica Nicotiana*—and a scientific 'academy', the *Academia Nicotiana Internationalis*, to buttress the fortunes of tobacco, then under siege from public health activists.¹¹

In 1953, a great deal of attention was given to an experiment by Ernst Wynder, Evarts Graham and Adele Croninger, showing that tumours could be generated by painting cigarette smoke tars onto the shaved backs of mice.¹² *Life* magazine devoted several pages to the story, and *Time* cited Graham's conclusion that the case against tobacco had now been proved 'beyond any doubt'.¹³ Public confidence in tobacco was shaken, and stock prices of American cigarette manufacturers plummeted. Tobacco manufacturers saw this new 'health scare' as a mortal threat to their livelihood, and decided to organise a response. On December 14, 1953, at the Plaza Hotel in Manhattan, CEOs of the six largest tobacco manufacturers in the USA (all but Liggett) met to plan a response. The outcome was a far-reaching plan to refute the accumulating evidence, using adverts, 'white papers', press releases and corporate schmoozing with popular science writers and journalists. Support for (industry-friendly) science was a vital part of this enterprise: cigarette manufacturers called for 'more research' to resolve a purported 'controversy', and set out to reassure the public that the companies were taking charge. That campaign was by and large a success, judging from the fact that per capita consumption rebounded from its dip in 1953. Cigarette consumption in the USA would in fact continue to grow throughout the 1960s and 1970s, peaking at about 630 billion sticks in 1982 before starting to decline.

Cellular pathology

A third line of evidence for the cigarette–cancer link came from cellular pathology. Pathologists in the 1930s had started noticing the capacity of cigarette smoke to cause ciliastasis—the deadening of the tiny whip or hair-like structures lining the upper airway passages, structures known to be responsible for wafting particulate contaminants out of the lungs.¹⁴ Suspicions started to grow that ciliastasis could cause cigarette smoke to become trapped in the lungs, causing cancer. Pathologists also started exploring whether damage from smoking could be discerned at the level of the cell. Anderson C Hilding in 1956 confirmed that smokers were experiencing pulmonary ciliastasis, but also that cilia were being deadened at precisely those parts of the lung where cancers were most likely to develop.¹⁵ Oscar Auerbach about this same time showed (from autopsy studies) that precancerous changes could be detected in the cells of smokers—even in those who had died from other causes.¹⁶

Cancer-causing chemicals in cigarette smoke

A fourth line of evidence stemmed from the discovery of cancer-causing chemicals in cigarette smoke. Polycyclic aromatic hydrocarbons had been identified as carcinogenic constituents of coal tar in the 1930s, and the question then arose: might there not be similar compounds in cigarette smoke? Angel Roffo in Argentina was the first to identify polycyclic aromatic hydrocarbons in cigarette smoke from their distinctive spectrographic signatures, and for a time at least his was the most authoritative voice in this realm.¹⁷ Roffo's work was taken seriously even by consultants working for the industry. In 1947, in an internal report to the Lorillard company, makers of Old Gold cigarettes, John B Fishel of Ohio State University acknowledged the presence of 'carcinogenic benzopyrene in tobacco tars', citing Roffo as an authority.¹⁸ Tobacco industry laboratories conducted their own investigations: Brown and Williamson researchers identified benzopyrene in cigarette smoke in 1952, and by the end of the decade cigarette manufacturers had characterised several dozen carcinogens in cigarette smoke, including arsenic, chromium, nickel and a veritable zoo of polycyclic aromatic hydrocarbons (chrysene, methylcholanthrene, dibenzanthracene, dibenzacridene, etc). As Philip Morris research director Helmut Wakeham put it in 1961, carcinogens were found in 'practically every class of compounds in cigarette smoke'.^{19 20}

The confluence of these diverse forms of evidence—from epidemiology, animal experiments, clinical observation and chemical analysis, combined with diminishing evidence for alternative explanations, prompted health and medical authorities throughout the world to publicly acknowledge a cigarette–cancer link. The American Cancer Society's National Board of Directors in 1954 announced 'without dissent' that 'the presently available evidence indicates an association between smoking, particularly cigarette smoking, and lung cancer'. The Public Health Cancer Association that same year advised stopping smoking as a way to prevent cancer, and cancer authorities in Norway, Sweden, Finland, Denmark and The Netherlands came to similar conclusions. UK cancer authorities came on board, as did the Joint Tuberculosis Society of Great Britain and Canada's National Department of Health and Welfare.²¹ Sceptics were converted, and medical attention shifted from the question of 'whether' to the question of 'how'—and what to do about it.

Researchers in the tobacco industry also became convinced of a cigarette–cancer link—though this was never admitted publicly. Claude Teague in his confidential 1953 'Survey of Cancer Research', written for upper management at RJ

Reynolds, makers of Camel cigarettes, concluded that the parallel rise in cigarette use and cancer had led to the suspicion that tobacco was 'an important etiologic factor in the induction of primary cancer of the lung'. Teague observed that clinical data were confirming the relationship, and concluded that the large body of animal experimental work 'would seem to indicate the presence of carcinogens'.²²

Teague was not the only tobacco insider conceding a hazard. Harris Parmele, Lorillard's director of research, in 1946 had commented privately on how 'Certain scientists and medical authorities have claimed for many years that the use of tobacco contributes to cancer development in susceptible people. Just enough evidence has been presented to justify the possibility of such a presumption'.²³ The American Tobacco Company in the summer of 1953 took the extraordinary step of sponsoring a series of secret animal tests in the laboratories of the Ecusta Paper Corporation, makers of much of the world's cigarette paper, with the goal of finding out whether it was the tobacco leaf or the cigarette paper that was causing all this cancer. Their conclusion, distributed only privately, was that tobacco—and not the paper—was the culprit.²¹

Tobacco industry insiders by the mid 1950s clearly knew their product was dangerous. In December of 1953, when Hill and Knowlton was exploring how to respond to the uproar surrounding the publication of carcinogens in cigarette smoke, one tobacco company research director commented in a confidential interview: 'Boy! Wouldn't it be wonderful if *our* company was first to produce a cancer-free cigarette. What we could do to competition!' Another remarked on how fortunate it was 'for us' (ie, for cigarette manufacturers) that smokers were engaging in 'a habit they can't break'.²⁴ The mid-1950s cancer consensus was clearly (albeit privately) shared by the companies; and the reality of addiction was also starting to be conceded—at least in internal industry documents.

UK cigarette makers also commented on the lung cancer consensus. Three leading scientists from British American Tobacco (BAT) visited the USA in 1958, for example, and found that with only one exception all of those consulted—including dozens of experts inside and outside the industry—believed that a cancer connection had been proved.²⁵ Alan Rodgman at Reynolds 4 years later confessed that while evidence in favour of the cancer link was 'overwhelming', the evidence against was 'scant'.²⁶ Helmut Wakeham at Philip Morris about this same time drew up a list of dozens of carcinogens in cigarette smoke.²⁰ None of this was made public; indeed the tobacco industry throughout this time and for decades thereafter—until the end of the millennium—refused to admit any evidence of harms from smoking. No one can say precisely how many lives were lost as a result, but if the decline in per capita consumption that began with the US Surgeon General's report in 1964 had begun instead in 1954, when the conspiracy to challenge the science was launched, millions of lives would have been saved.²⁷

The 1964 Surgeon General's report, which recognised smoking as a cause of lung cancer in men, is often regarded as a turning point in the recognition of health harms from smoking. But the Surgeon General's report was actually a kind of scientific anticlimax: from an evidentiary point of view the case against smoking had been closed by the end of the 1950s, and it was only the truculence and obstinacy of cigarette manufacturers that forced a blue-ribbon review by the federal government. Charles S Cameron, Medical and Scientific Director of the American Cancer Society, put the matter nicely in a 1956 overview for the *Atlantic Monthly*, noting that if the same level of evidence had been

arrayed against, say, spinach, no one would have objected to the banning of that plant from the national diet.²⁸

POPULAR KNOWLEDGE—AND IGNORANCE

History is, among other things, the study of origins and outcomes—how things come to be and disappear. The presumption is often of a certain contingency: how things turn out is often the outcome of struggles among competing agents. We've reviewed here the rise of scholarly knowledge of cigarette carcinogenicity, but it is also important to realise that popular knowledge, too, has a history. Scholars don't pay enough attention to what non-scholars think about the world, the proper study of which is agnology.²⁹ What is the history of popular knowledge of the tobacco lung cancer link? What efforts have been made to generate ignorance?

One source of information for the history of ignorance is the polling data amassed by professional opinion research agencies and their tobacco industry counterparts. In 1954, for example, George Gallup sampled a broad swath of the US public to ask: 'do you think cigarette smoking is one of the causes of lung cancer, or not?' 41% answered 'yes', with the remainder answering either 'no' or 'undecided'.³⁰ Even large numbers of doctors remained unconvinced. In 1960, in a poll organised by the American Cancer Society, only a third of all US doctors agreed that cigarette smoking should be considered 'a major cause of lung cancer'. This same poll revealed that 43% of all American doctors were still smoking cigarettes on a regular basis, with occasional users accounting for another 5%.³¹ With half of all doctors smoking, it should come as no surprise that most Americans remained unconvinced of life-threatening harms from the habit.

The tobacco industry was not innocent in this persistence of ignorance. Cigarette makers spent countless sums to deny and distract from the cigarette–cancer link, in some instances actually quantifying the impact of their denialist propaganda. In 1973, for example, the Tobacco Institute hired AHF-Basico Market Research Co. and Audience Studies, Inc., to measure the impact of its 1972 propaganda film, 'Smoking and Health: The Need to Know', shown to hundreds of thousands throughout the country, including high school students. Prior to screening, viewers were asked a series of questions about whether the Surgeon General 'could be wrong about the dangers of smoking'; the same questions were then asked after the screening. Anne Duffin at the Tobacco Institute was happy to report that the film had reduced by 17.8% the number of people agreeing that 'Cigarette smoking cause[s] lung cancer' (from 74.9% to 57.1%). The film had also produced 'significant shifts' in attitudes favourable to the industry in other areas, including whether recent reports had 'overemphasized the dangers of smoking'.³²

Global denialist campaigns have borne similar fruit. In the 1980s, UK tobacco researchers commented on how Philip Morris was piloting a 'global strategy' to deny the reality of secondhand smoke hazards, spending vast sums of money 'to keep the controversy alive'.³³ Hundreds of millions of Chinese remain poorly informed about the hazards of smoking, and as recently as 2011, scholars from the International Tobacco Control Policy Evaluation Project in The Netherlands published a survey showing that only 61 per cent of Dutch adults agreed that cigarette smoke endangered non-smokers.³⁴

THE GLOBAL TOLL

The cigarette is the deadliest artefact in the history of human civilisation.²¹ Consumption rates are falling in most of the richer

countries, but smoking rates remain high or even increasing in many parts of the globe. In China, cigarette consumption has risen from about 500 billion 1980 to over four times that in 2010, and it is not yet clear whether consumption has peaked. China is now manufacturing about 2.4 trillion cigarettes per year, close to 40% of the global total. Consumption has been facilitated by the introduction of ultra high speed cigarette making machines: Hongta's Yuxi Cigarette Factory, for example, produces over 90 billion cigarettes per year, using 52 high-speed Molins cigarette making machines. Modern cigarette making machines of the sort made by the Hauni Corporation in Hamburg or GD (Generate Differences) in Bologna crank out cigarettes at rates up to 20 000 per min, which helps account for the dramatic drop in manufacturing costs over the last century or so. Cigarette factories today produce death at a faster

rate—and cheaper—than any previous form of industrial manufacture. If cigarettes cause 1 lung cancer for every 3 or 4 million smoked,³⁵ this means that a factory such as Hongta's in Yuxi is responsible for generating 25 000 or 30 000 deaths per year from lung cancer. And about twice that number from other diseases. There are about 400 industrial-scale cigarette factories in the world,³⁶ each of which causes thousands of preventable deaths per year (see box 1 and table 1).

There are still many myths surrounding smoking—that the dangers have long been 'common knowledge', for example, or that legitimate scholarly doubt about the reality of hazards postdates the Surgeon General's report of 1964.^{37–39} Yet another myth, though, is that the tobacco 'problem' has by and large been 'solved'. Tobacco is commonly referred to in the past tense—as when critics of the fast food industry talk about solving dietary problems 'the way the tobacco problem was solved'. The fact is that cigarette use persists, and on a massive scale. Global cigarette use seems to have peaked at about 6 trillion cigarettes sometime after the turn of the new millennium, but the deadly effects of this epidemic will still be felt for decades—even if global use continues to decline. Only about 100 million people died from smoking in the 20th century, whereas several times that are likely to die in the present century, even if current rates of smoking fall dramatically.³⁵ Most of the tobacco epidemic remains in the future, with the total global toll likely to approach 2 million lung cancer deaths per year in the 2020s or 2030s.

No causes are themselves uncaused, however, which means that when we think about what causes lung cancer or even smoking, we should think not just in terms of how individuals 'decide' to start smoking, but rather in terms of larger, more weblike threads of causation. We have to look at the cigarette epidemic—and therefore lung cancer—as facilitated by long causal chains of a sociopolitical, technical, molecular and agricultural nature. If cigarettes cause cancer, then so do the machines that roll cigarettes and the companies that supply the 'filters', 'flavourants' and paper. We have to realise that adverts can be carcinogens, along with the convenience stores and pharmacies that sell cigarettes. The executives who work for cigarette companies cause cancer, as do the artists who design cigarette packs and the PR and advertising firms that manage such accounts. Farmers who grow tobacco are part of this

Box 1 What is a human life worth to a cigarette manufacturer?

Cigarettes cause about one death per million smoked³⁵ with a latency of about 25 years, which is why the 6 trillion smoked in 1990 will cause about 6 million deaths in 2015. That's one death every 5 seconds. One-third or one-quarter of those deaths will be from lung cancer; about one every 15 or 20 s.

This relationship is fairly consistent in different parts of the world, given the homogeneity of cigarettes and how similarly they are smoked. It also means we can generate some interesting equivalences. Cigarettes typically come in 20 sticks per pack, with 200 sticks per carton, 10 000 sticks per master case and 10 million sticks per container. A 12 m (40 ft) container of the sort shipped overseas or trucked by highway houses 10 million cigarettes, which means that each container will cause about 10 deaths.

We can also think about this in terms of the rate at which cigarettes are smoked. A total of 6 trillion cigarettes are smoked every year, and if each cigarette is about 60 mm (counting only the part that is smoked), this means that 360 trillion mm of cigarettes are smoked per year. Converting this, 360 trillion mm is 360 billion m, or 360 million km. Imagined as one long rod, this means that cigarettes are smoked at a rate of 360 million km per year, which is more than 10 km/s. Cigarettes are smoked at a rate equal to the speed at which satellites orbit the earth.

We can also think about the deaths caused per unit weight of stuffing. Cigarettes contain about two-thirds of a gram of tobacco, which means that if it takes 3 million cigarettes to cause one lung cancer, it takes about 2 million g—or 2 metric tonnes—to cause one lung cancer. A typical tobacco farm yields about 2 tonnes per hectare, so a 10-hectare field will cause about 10 lung cancer deaths/year. And 20 additional deaths from heart attacks, gangrene of the feet, cancers of the bladder and oral cavity, etc.

Finally, we can also think about this in terms of the value of a life as assumed by tobacco manufacturers. Cigarette companies make about a penny in profit for every cigarette sold, or about US \$10 000 for every million cigarettes purchased. Since there is one death for every million cigarettes sold (or smoked), a tobacco manufacturer will make about US\$10 000 for every death caused by their products. Otherwise put: a cigarette manufacturer will not forgo US\$10 000 in profit, even if this means the death of one of their customers. The value of a human life to a cigarette manufacturer is therefore about US\$10 000.

Table 1 Factories of death (selected)

	Cigarettes produced/ year (year)	Deaths caused per year
Philip Morris's Richmond plant	146 billion (2010)	146 000
Philip Morris Holland, Bergen op Zoom, The Netherlands	96 billion (2006)	96 000
Yuxi Cigarette Factory, Yunnan	90 billion (2008)	130 000
Kunming Cigarette Factory, Kunming, China	71 billion (2010)	71 000
Philip Morris Izhora Cigarette Factory, St. Petersburg	70 billion (2011)	70 000
Hong He Cigarette Factory, Yunnan, China	65 billion (2005)	65 000
Anyang Cigarette Factory, China	50 billion (2008)	50 000
Hongyun Cigarette Factory, Qujing, Yunnan	47 billion (2008)	47 000
Thane Road, Nottingham (Imperial Tobacco), UK	50 billion (2003)	50 000
Hangzhou Cigarette Factory, China	47 billion (2007)	47 000
Reemtsma, Berlin	36 billion (2005)	36 000
Philip Morris Kuban, Russia	33 billion (2002)	33 000

What this paper adds

- This paper reviews the converging lines of evidence that led to the recognition that smoking is the major cause of lung cancer.
- It also shows that the non-scholarly public was slower than scholars and medical professionals to recognise tobacco harms.
- The point is made that part of that lag can be traced to campaigns mounted by the industry to manufacture doubt.
- The point is also made that global tobacco use would be declining were it not for China, which now accounts for about 40 percent of all cigarettes sold (and smoked).
- Deaths caused by some of the world's largest tobacco factories are calculated, and the value of a human life for a cigarette manufacturer is shown to be about \$10 000.

network, as are the politicians who take money from 'Big Tobacco', and those chemists and breeders who favour the nicotine molecule. So too must we include those many hundreds of experts who testify for the industry in court.²¹ We need to better understand such webs or networks if we are to be more creative in finding ways to reduce the toll from this, the world's deadliest malignancy.

Competing interests The author has served as an expert witness in litigation against the tobacco industry.

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Correction

Proctor RN. The history of the discovery of the cigarette–lung cancer link: evidentiary traditions, corporate denial, global toll. *Tob Control* 2012;**21**:87-91. The data related to ‘Yuxi Cigarette Factory, Yunnan’ in Table 1 was misprinted. The correct table should appear as below:

Table 1 Factories of death (selected)

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Yuxi Cigarette Factory, Yunnan	90 billion (2008)	90 000
Kunming Cigarette Factory, Kunming, China	71 billion (2010)	71 000
Philip Morris Izhora Cigarette Factory, St. Petersburg	70 billion (2011)	70 000
Hong He Cigarette Factory, Yunnan, China	65 billion (2005)	65 000
Anyang Cigarette Factory, China	50 billion (2008)	50 000
Hongyun Cigarette Factory, Qujing, Yunnan	47 billion (2008)	47 000
Thane Road, Nottingham (Imperial Tobacco), UK	50 billion (2003)	50 000
Hangzhou Cigarette Factory, China	47 billion (2007)	47 000
Reemtsma, Berlin	36 billion (2005)	36 000
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