Women and health

Screening
Overdiagnosis,
Cancer:
What are we talking about?

Francesco di Simone da Santacroce 1440 Musei Civici

Bruxelles 7 nov 2019

Bernard Duperray

A web of conflicting information

- For more than a century periodically claims to have techniques to defeat breast cancer: surgery, radiotherapy, chemotherapy, mammography screening, etc. But in fact, nothing has happened and goes as planned.
- Breast cancer is still one of the first killers among female cancers.
- The astonishing aggressiveness of medicine towards women in the treatment of breast cancer has proven counterproductive. Yet practices persist.
- What seemed intuitively obvious an earlier diagnosis thanks to the mammography saves lives was contradicted by screening.
- The bankruptcy of the screening brings to the fore the divorce between the affirmation of a success and a deeply deleterious reality.
- This failure imposes a total questioning of the links between the woman, cancer and medicine.
- Everything shattered.

Appearance and reality

- The woman: a stack of organs animated by a divine spark ... or a member of a species conscious of its belonging to nature from which it can not be dissociated?
- Breast cancer: an intruder that must be riddled as soon as possible ... or a component of life that must be understood connections before deciding his fate?
- Medicine: a body of knowledge at the service of human well-being ... or an insatiable ogress who feeds on patients and even on well-being to build an expanding market in search of profit?
- The controversy over the detection and management of breast cancer stems from the fact that medicine denies women the right to be actors in their healing and completely replaces them in the name of a science they can not control. not yet.

Wife...

Woman has a changing social and personal status throughout history

The social treatment of the breast is a good reflection of the feminine condition. The breast is both the organ of breastfeeding as in all mammals and a very specific organ of the human species by its emblematic erotic role of femininity.



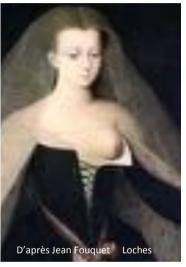
150 million years: the mammals. 45 million years: the first monkeys. 20 million years. hominids. 7 million years: bipedalism. 3 million years: the first tools (the choppers). 1.8 million years: the end of estrus the human hand, Prehistory: the female breast. Thus the

human species is forged..



Venus of Willendorf (24,000 years old)

The opulent chest of Paleolithic Venus is in the foreground, carved in a ritual of fertility or eroticism?



The word sein appears in the french language with courtly love in the 12th century.

At the Renaissance. the beauty hitherto of divine order becomes human.



But it is also the time of witchcraft trials and paintings of St. Agatha that testify to an incredible violence against women.



Today, the breast is commodity

E A SAUVÉ

Pink October displays his contempt for the woman and the female body.

Business and lies.



The woman has been at the center of human activity for millennia

Upper Paleolithic

Neolithic

Archaic Greece etc ...

The woman is at the heart of life

The deities are women

The descent is matrilineal

It's the time of the mother goddesses



Lady with Leopards, Çatal Höyük (Turkey), 8th millennium BC J. - C. The agriculture develops.
The woman collects the product of labor and administers the common good.



Mother goddess
Veneration of
Motherhood
(Mesopotamian
Civilization)
The woman and her
breasts are in front of
the stage.



Demeter: goddess of fertility, of the earth.

In archaic Gentile Greece the divinities are still feminine. In matrilineal societies, the woman has the full disposition of her body, she has no husband, the child has no father but an uncle.

There are still many traces in the world. The Na, in China, are still a living example.

The terms matriarchy and patriarchy may be reminiscent of a simple reversal of power relations when they involve radically different societies.

Antiquity is for women descent into hell

(From matrilineal descent to patrilineal descent)

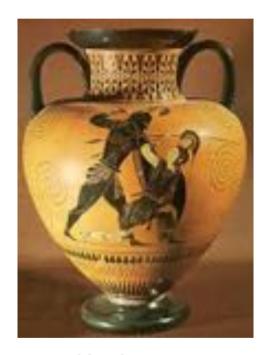
Patriarchy imposes itself with the appearance of private property. The woman is submissive and loses her autonomy. Reduced to her uterus, she ensures filiation that concentrates the tools and wealth accumulated by man.

The reciprocal social situation of men and women results from the tools that they hold.



With the "patriarchy", the female body is devoted to cutting, on one side the uterus sequestered in the gynaeceum on the other a body devoted to pleasure with hétaïrisme.

Zeus dismisses from Olympus the female deities. The Greek language in the classical period evolves: "master" takes the meaning of husband, "tamed" becomes the wife.
Asclepius (Aesculapius) replaces his mother Coronis, previously seen as the mother of medicine.



A painful evolution: mythology and folk tales testify to a centuries-old struggle between matriarchy and patriarchy.

Achilles, in spite of his emotion, kills Panthesilea.

Karkinos or carcinoma

The word karkinos or crab appears with Hippocrates (460- 370 BC) to clinically designate a tumor process. But descriptions of breast cancer are present well before, from ancient Egypt around 2600 BC.

From the nineteenth century its definition is reduced to a single point image seen under the microscope.

Breast cancer has a singular place among all cancers.

It is one of the first identified because it sits in an external organ easily accessible to clinical examination.

Present in both sexes, (1 to 2% in men), breast cancer is essentially feminine.

Papyrus Ebers Imhotep (2600 BC) The first description of breast cancer

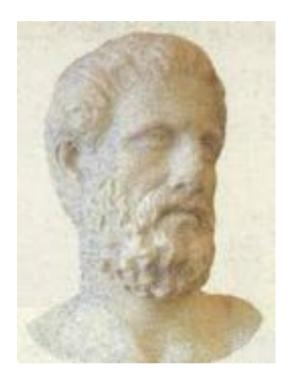


Atossa Queen of Persia breast cancer has been described 475 BC



Medicine

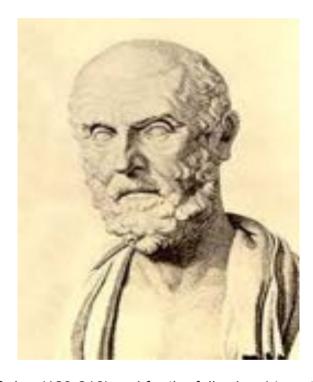
Antiquity is also the advent of modern medicine.



Hippocrate (460-370 BC):

On the one hand, the Hippocratic revolution:

The disease is no longer due to supernatural forces. One observes and seeks in the body the cause of the evils to deduce the possible treatments. Hippocrate warns about what may seem intuitively obvious.



Galen (129-216) and for the following 14 centuries:

On the other hand, men's medicine in a patriarchal society sees women as: ... "just as, of all animals, man is more perfect, so in the human species man is more perfect than woman. The woman is "only a male upside down" a receptacle, an empty vase,

the sperm retained in the testicles (female) of the woman is poor and cold unable to engender. The woman is just good at sheltering the male seed that is really fertile. "

Since ancient times, a disproportionate aggressiveness towards the female body.



Mastectomy scene in 1668

"Women utter such cries that they can discourage the most tenacious surgeon and prevent the operation. To do this, the surgeon must be unwavering and not allow himself to be troubled by the patient's crying. (Lorenz Heister, an 18th century surgeon)

Violence in a well-established tradition:

"I will increase the suffering of your pregnancies, you will give birth with sorrow, and your desires will come to your husband, but he will rule over you" (Genesis).

Code Napoleon 1804:

"Persons deprived of legal rights are minors, married women, criminals and mentally deficient". "The woman and her womb are the property of man" ...

At the end of the 19th century, the medical institution persists and signs.

"A woman can not claim to seriously go through a medical career (...) unless she ceases to be a woman: by physiological laws, the female doctor is a dubious, hermaphrodite, or sexless being, in any case a monster. The one that this distinction will attract is free to try to acquire it. "Lucas-Champion, Just," article 9997 "J. med.chir.prat., No. of June 1875. pp. 241-242

"To be a doctor one must have an open and prompt intelligence, a solid and varied instruction, a serious and firm character, a great composure, a mixture of goodness and energy, a complete empire over all his sensations, a vigorous moral, and if necessary, muscular strength. (...) Are not they the opposite of feminine nature? Richelot, G. The woman-doctor, Paris: E. Dentu, 1875, p.43 and following.

It is in this context that, in 1894, Halsted, a renowned North American surgeon, claims to obtain healing through enlarged breast removal.

He resumes the classic pattern of locoregional and then general progressive organ disease.

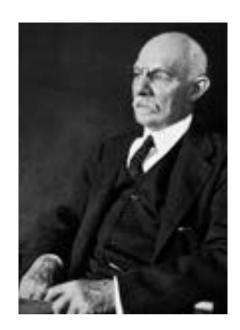
A small tumor corresponds to an early diagnosis synonymous with curable.

Any delay in diagnosis is detrimental to the patient.

The breast is the ideal organ for this scheme: it is external and not vital, which seems to facilitate diagnosis and treatment.

The progress of the surgery at the end of the nineteenth century, in which Halsted participates, allows women to no longer die on the operating table.

So everything seems to come together to defeat breast cancer.



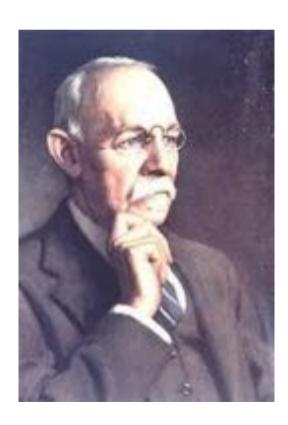




Halsted has pushed to the extreme the removal of the breast and its environment, achieving a real mutilation with heavy chest sequelae and sometimes a disabling big arm. But it was the price to pay to heal.

In 1894, William Halsted announced three recurrences after 50 interventions, that is a remarkably low rate of only 6%.

With the announcement of Halsted begins in the industrialized countries the generalization of radical surgery as a treatment for breast cancer.





For the Halstédienne way of looking, which is always the reference :

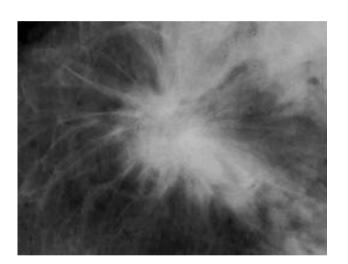
- Small volume lesion means early diagnosis.
- Small and early are synonymous with curable.
- The progression of the disease is inevitable and linear in time:
- Atypical cell> carcinoma in situ> invasive cancer> metastases> death
- Everything is linked in successive stages.
- It is therefore necessary to interrupt as quickly as possible this infernal mechanics.

The arrival of mammography in the 1950s / 60s should give the finishing stroke to cancer by making its diagnosis possible at its very beginning

It only remained to do...

screening!





"Showing my breasts, I have protected my life, do like me, have a mammogram"

Especially since: TWO EXPERIENCES RANDOMIZED SCREENING are supposed to have proven the effectiveness of mammography and thus validated the Halstedian schema of the natural history of the disease.

- HIP, New York, 1963.
- The Two Counties: Sweden, 1985, 1997.

The published results are identical:

Mortality drop by 30% in the screened group compared to the control group in women over 50 years old.

In view of these results, it seemed intuitively obvious that breast cancer screening allowed for earlier diagnosis, hence better chances of remission or even cure.

The expected result was a drastic drop in mortality, the eradication of advanced forms and a decrease in the number of total mastectomies.

The adverse effects of screening were considered marginal, given the expected benefits.

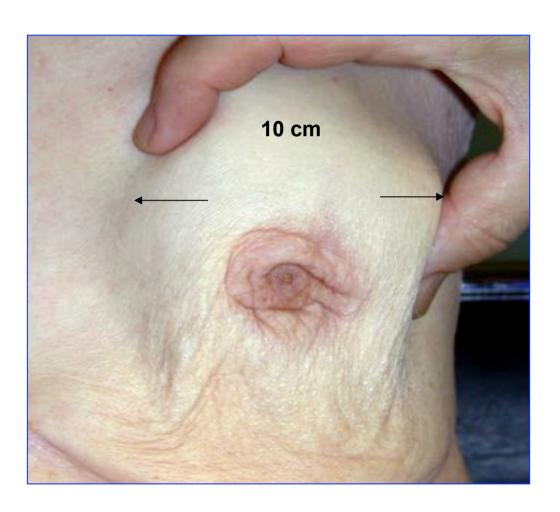
The reality has turned out to be different.

Mammography is only a picture without preparation of soft parts an overestimated technique to demystify

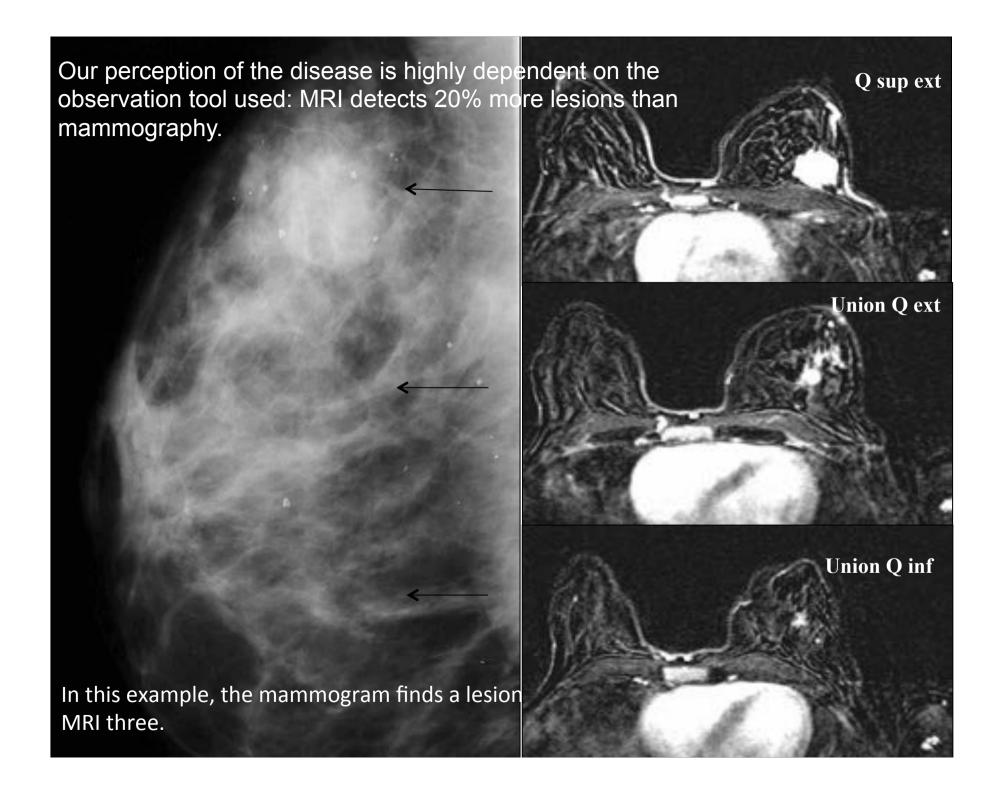
Cancer cells do not differentiate from normal cells in mammography. These are essentially indirect signs related to the reaction of the surrounding tissues that make the malignancy suspect.

Mammography only detects certain cancers and the tomosynthesis does not change anything.





Tumor palpable 10 cm without radiological translation



Looking closer!

The detailed examination of the interventions practiced by Halsted until May 1892, for which the wait time was at least 2 years, shows that 16 of the first 25 women, 64% had recurred or died.

Contrary to Halsted's claims, his intervention is a failure.

It was not until the 1970s and 1980s that Fisher and Veronesi questioned Halsted's hypothesis by randomized studies and advance a hypothesis alternative:

There is no order in the spread of the tumor.

Variations in treatment do not affect survival.

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In addition, clinical practice teaches us that:

Small does not mean early diagnosis and does not necessarily imply good prognosis.

Big does not exclude early diagnosis.

The efflorescence of cancer diagnoses in situ is not accompanied by a decrease in number of invasive cancers.

In situ cancer can be palpable.

In 40 years, the time between two screenings has steadily decreased: 3 years then 2 years in France and 1 year in the USA without the cancers of the interval being mastered.

Progression of the disease is neither inevitable nor linear. No mechanical chaining exists between different states : in situ, invasive etc ... (stagnation and regression are possible)

In fact, randomized studies do not provide evidence of a decrease in mortality from screening.

The Lancet in 2000, the Cochrane in 2001 and 2011, Prescrire in 2006 and 2007 call into question the reality of a 30% mortality decrease.

The testing methodology does not meet the current quality criteria and <u>no trial in favour of screening reaches the acceptable</u> level when considering :

- draw method,
- comparability of groups,
- exclusions during study after randomization
- classification bias of causes of death for the groups screened

Screening is not associated with a proven decline in breast cancer mortality

Breast cancer deaths by whether or not the group is screened for mammography after 7 years

Result of the 3 most reliable controlled trials (These results are confirmed at 25 years old)

Malmö: n = 42283; Canada I: n= 50430; Canada II: n= 39405

Study and reference	Invitation to a mammogram	
	yes	no
NA a line ii ra	4.4	20
Malmö [Andersson I, BMJ 1988]	44	38
Canada I [Miller AB, CMAJ 1992]	38*	28
Canada II [Miller AB, CMAJ 1992]	38	39
_ ,	100	405
Total, 7 years	120	105

15 more breast cancer deaths in the group being tested

^{*} An audit confirmed these results : no bias [Bailar JC CMAJ 1997]

The two baseline studies for screening are unreliable.

Results of the Two-County trial of mammography screening are not compatible with contemporaneous official breast cancer statistics in Sweden.

Dan. Med. Bull. **2006**; 53: 438-40.

ZAHL PH et coll

These researchers show in particular that the published results concerning the Two Counties trial are <u>incompatible</u> with the data of the Swedish national file!

"Compared to Swedish official statistics, we found that 192 breast cancer cases and 43 breast cancer deaths do not seem to be included in the main publication of the Two-Counties trial". "In 1992, Tabar and his colleagues reported 465 breast cancer deaths in the 40 to 74 age group, 16 less than the number reported in the Swedish trial overview" etc.

Catherine Riva et al reported in 2012 in The Lancet the interests of László Tabár, instigator and investigator of the Swedish trials.

In fact, none of the objectives of screening have been achieved:

1) Screening does not cause a drop in mortality

Evolution of standardized rates of breast cancer mortality in France during the last 60 years.



Mortality rates continued to increase until the 1990s despite screening.

From the 1950s to the 1980s, before organized screening, the size of tumors at the time of diagnosis had already changed from "plum to nucleus" while mortality rates continued to grow.

Despite the introduction of screening from the 1980s, mortality rates have steadily increased until 1993.

To those who rave about the decline in mortality that has been going on for years 90, it should be recalled that current mortality rates are comparable to those in the 1950s, and that decline can not be attributed to screening. Indeed:

Screening is not responsible for the current mortality decline.

Many studies confirm the lack of link between the activity mammographic and breast cancer mortality decline :

- Norway (Kalager, NEJM 2010) regions with / without screening
- Denmark (Jorgensen, BMJ 2010) regions with / without screening
- Europe (Autier, BMJ 2011) three pairs of countries with / without screening
- France (Junod, BMC Cancer 2011) before / after screening

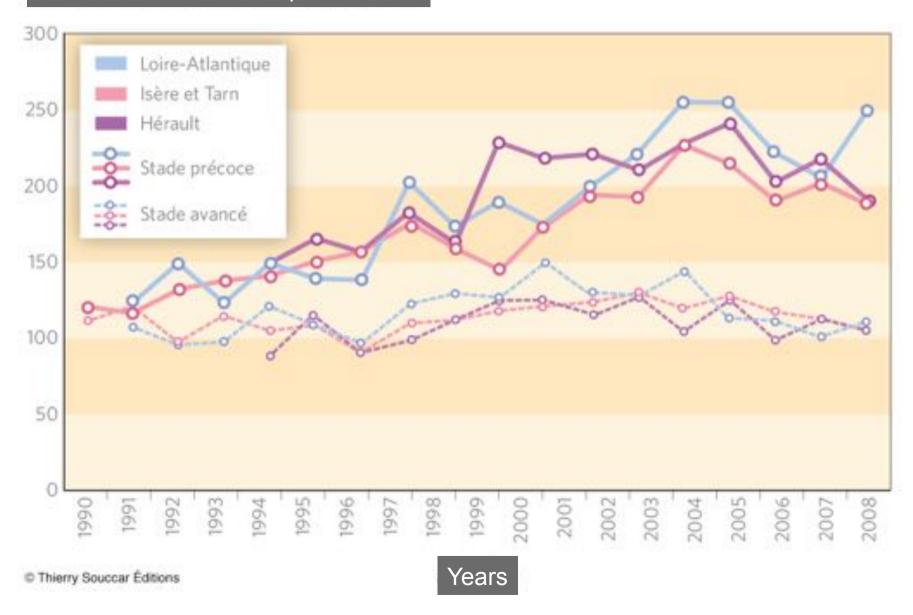
A study, done in the United States by a team from Harvard University in Cambridge, of sixteen million women followed for ten years between 2000 and 2010 in 547 counties shows that the extension of the screening was not accompanied by a decrease specific mortality.

P. Autier confided to the magazine *Le Monde* at the end of October 2011:

"When I started working on this topic, I was convinced that the screening was effective. But, obviously, there is a gap between test results and what is observed in the populations."

2) Screening does not diminish the number of advanced forms

standardized incidence per 100,000



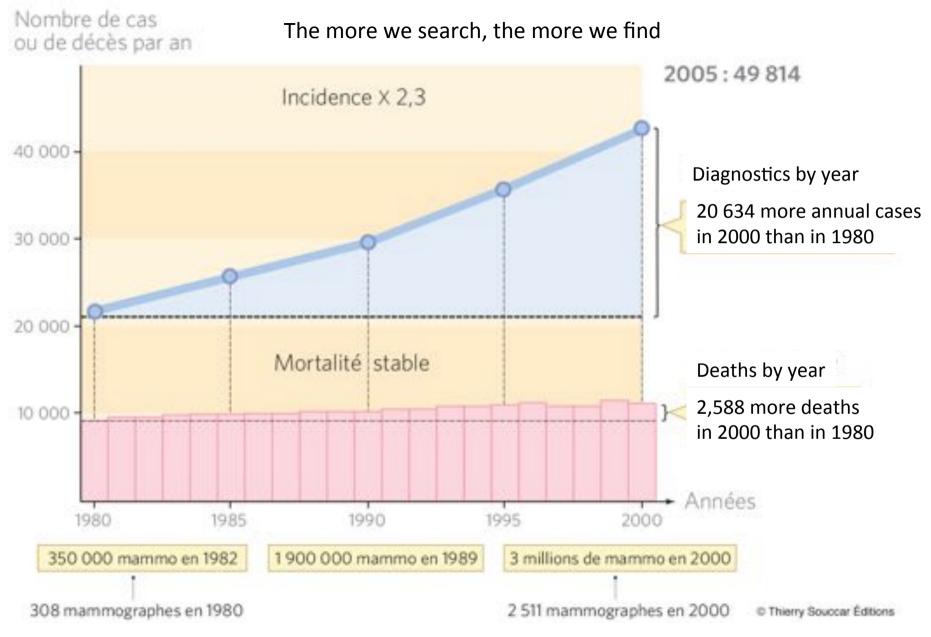
3) Screening does not decrease the number of total mastectomies

Evolution in France of the number of mastectomies between 2000 and 2016



None of the objectives of the screening were realized.

Not only is screening proving ineffective, but it is counterproductive.



Epidemic or overdiagnosis

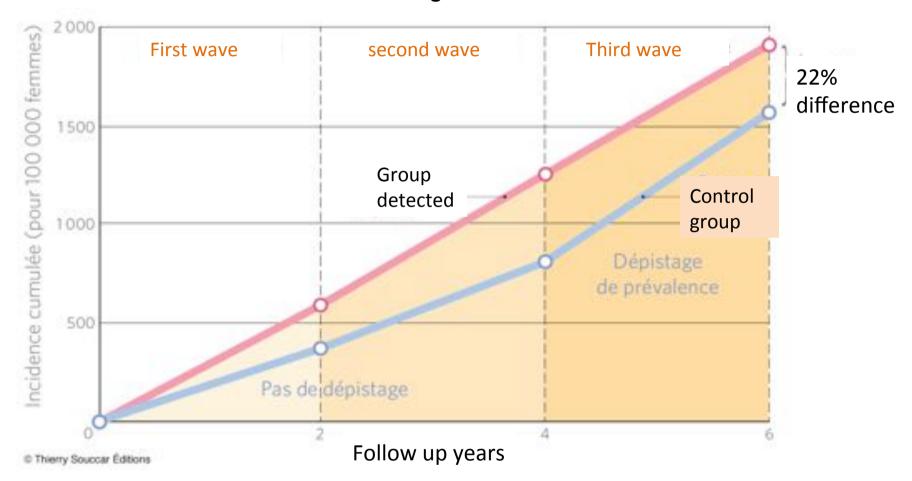
The hypothesis of an epidemic does not hold

If this continued increase in new annual diagnoses corresponds to an epidemic of lethal cancers, the mortality reduction should be considerable thanks to screening, (One would have cancer cured for one death in 1980 and three cancers cured for one death in 2000).

Neither the most optimistic results of controlled trials for mortality reduction nor therapeutic progress during this period can support this hypothesis.

How to explain this scissors phenomenon between the incidence which increases considerably and the mortality which remains almost stable?

A surprise guest settled without the knowledge of everyone at the screening table : overdiagnosis



Overdiagnosis is cancer "in excess" that is even more numerous than screening is more intense.

Example (Oslo 2006): the cumulative rate of cancer is 22% higher in the group screened every two years compared to a group detected once after 6 years.

Overdiagnosed cancer is a real cancer under our current definition of cancer, which is based solely on the histology of the tumor. But its evolution is atypical or occult compared to the expected pattern.

In the context of our current knowledge, this is not a diagnosis error, it is a correct diagnosis but not useful for the patient.

Reality of overdiagnosis

Its reality is highlighted by epidemiology by comparing populations with variable intensity screening.

In Norway, there is a precise individual follow-up of each woman. It is known how often each was examined by mammography.

Comparing those examined at regular intervals with others, we find that the cumulative breast cancer mortality over several years is the same in both groups.

On the other hand, the number of diagnoses of cancer is even higher than women had more often a screening mammogram.

The concept of overdiagnosis is supported by the result of systematic autopsies and breast reduction interventions for aesthetic purposes. The proportion of women carriers of asymptomatic cancers is much greater than expected.

110 systematic autopsies

(Nielsen study, Denmark, 1987)

Mammography and histological study of the breasts of women 20 to 54 years old with no history of breast pathology show:

20% malignant lesions including 2% invasive, (20 per 1000).

7% atypical hyperplasia, 37% of breast cancers between 40 and 54 years, 39% of breast cancers between 40 and 49 years old.

The reservoir of overdiagnosis is immense.

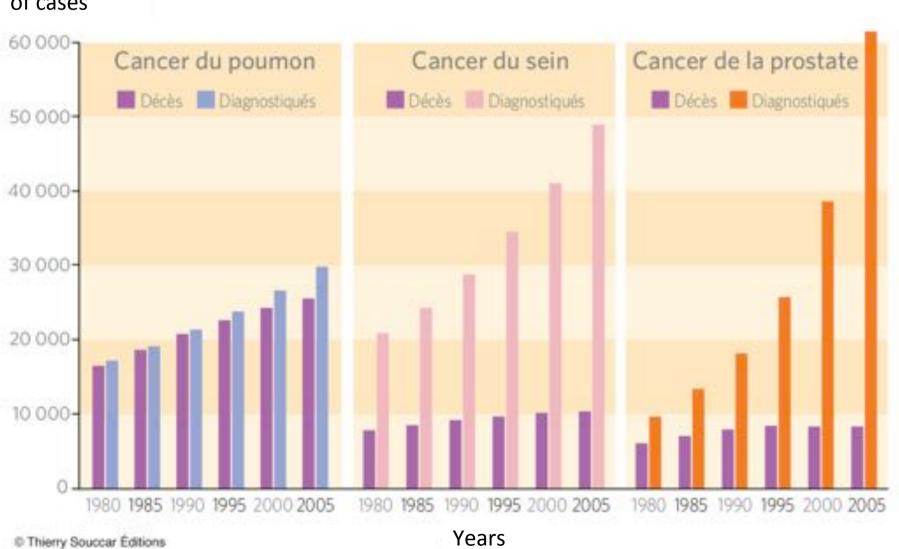
Problem!

Overdiagnosis is not identifiable by the radiologist, the caregiver, the pathologist, or the patient. For them, there are only diagnoses.

- Overdiagnosis explains why, despite the apparent success of treatments, screening does not cause a reduction in mortality in the population.
- With overdiagnosis, screening has become an autonomous entity that
 lives on healthy women subject to a market in full expansion where conflicts of
 interest dominate the "scientific" debate.

Evolution of incidence and mortality for three cancers (in France, from 1980 to 2005)





The apparent increase in incidence is mainly due to overdiagnosis, even if environmental factors also intervene.

- Mutagenic toxicants, endocrine disruptors, treatments like HRT, obesity, alcohol, delicatessen, red meat ... induce an increase in tumor lesions. Among these lesions, all will not be fatal cancers but they have been determining for decades a progressive growth of the impact.
- However, with the introduction of screening, there is a brutal and vertiginous increase in the number of cancers that is linked to overdiagnosis.

Quantification of overdiagnosis attributable to mammography screening in organized programs

- 1) Meta analysis of data collected from the 5 best-researched organized screening programs to allow quantified estimation.

Study of trends in breast cancer incidence before and after introduction of screening :

Data were collected over periods of at least 7 years before and 7 years after screening has been set up, so that the estimate is not distorted by the peak prevalence at the introduction of screening.

Age groups screened and not screened were included.

The increase in the incidence of breast cancer is closely related to the introduction screening and little of this increase is offset by a decrease in older women previously screened.

The increase in the incidence of breast cancer due to organized screening is estimated at :

- . **52%** (CI = 95%, 46 to 58%) when in situ are included,
- . 35% (CI = 95% CI, 29% to 42%) when only infiltrating carcinoma is taken into account.

- 2) Other study: Zackrisson S et al: Rate of overdiagnosis of breast cancer 15 years after end of Malmö mammographic screening trial: follow up study BMJ 2006 332: 689-692

Overdiagnosis estimated at 48.3% in women aged 35 to 84 and 38.6% if in situ is excluded.

- 3) Confirmation by a more recent study : Philippe Autiera, Mathieu Boniola, Mammography screening : A major issue in medicine ☆ European Journal of Cancer Volume 90, February 2018, Pages 34-62.

Overdiagnosis: 52% of cancers screened would be overdiagnosed.

Overdiagnosis mystifies the doctor

The confusion between lethality rate and mortality rate masks the reality of overdiagnosis and misleads the clinician.

Lethality rate: Number of deaths reported as a proportion of breast cancer diagnoses.

The increase in diagnostic activity (screening) leads to an increase in prevalent cases and overdiagnosis drowned in the mass of diagnoses, thus contributing to the decrease in the lethality rate.

This is the clinician's perception of the disease in an individual.

Mortality rate: number of deaths reported to the entire population. This really measures the <u>effectiveness</u> of a public health operation.

This is the epidemiologist's perception of the disease **in population**.

Facts observed in France Temporal evolution (1980 - 2005)

Rate per 100,000 women 35 years and over

Standard population : France 1992

	<u>1980</u>	<u>2005</u>
Incidence (invasive breast cancer)	153.1	269.1
Lethality in % (= mortality / incidence)	39.4 %	22.6 %
Mortality by breast cancer	60.4	60.8

Overdiagnosis mystifies women

Overdiagnosed women can not be identified and therefore question their overtreatment and its harmful consequences.

On the contrary, cured because they are not sick, these women are often, in fact, the spearhead of pro-screening while they are doubly victims, in their flesh and in their illusions that lead them to defend those responsible for their misfortune.

Screening has unacceptable deleterious effects

Screening for breast cancer **generates disease** in healthy women, which is a shame for a public health operation.

Overdiagnosed cancers cause **intolerable overtreatment** because of the major side effects it can cause.

(Clinical trials are mostly tested in men. Regardless of the principle tested, women are twice as likely to experience side effects as men.)

Overdiagnosed cancers increase the number of women considered to be risk group and also impact their offspring.

Overdiagnosis is also **provider of illusions**. This is because it is more common among the small tumors without ganglionic invasion it gives the illusion of the effectiveness of early diagnosis, screening and treatment. He disorients the research.

Screening is the source of unnecessary and dangerous irradiation.

Overdiagnosis is the cause of recurrent disinformation

- The unbalanced information about breast cancer screening is about consequences of erroneous ideas on its effects.

A study of American and European women showed that: 68% of them thought screening reduced their risk of getting 62% that screening reduced mortality by at least half 75% that 10 years of screening saved 10 out of 1000 participants (overestimation of 20 times in the best case).

- Another study showed that only 8% of women questioned were aware that participation in screening could harm women in good health.

 There is a conflict of interest when those who are in charge of provide information are responsible for success screening program.



"Lying and credulity mate and generate opinion." Paul Valéry

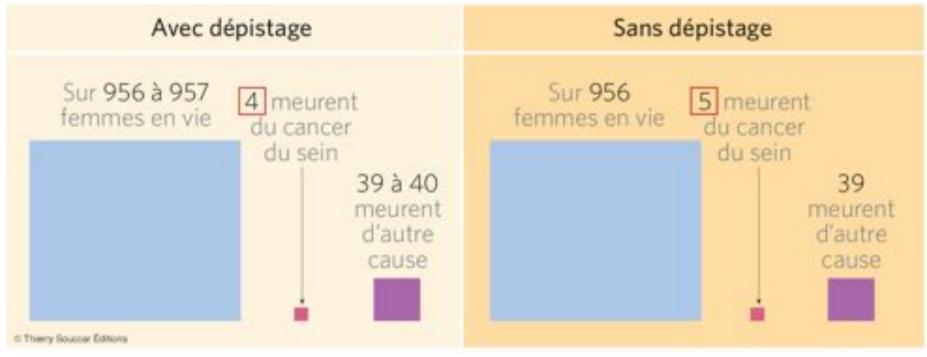




"Showing my breasts, I have protected my life, do like me, have a mammogram"

Disinformation: the art of manipulating opinion

To say that the risk of dying from breast cancer falls by 20% in screened versus non-screened women does not mean that one in five women will benefit from being tested. Information about the actual benefit that a woman will gain from screening only makes sense after conversion of the relative risk variation to the change in the absolute risk of dying from breast cancer in the absence of screening.



N. Biller-Andorno, P. Juni, Abolishing mammography screening programs? A view from the Swiss Medical Board. N Engl J Med, 370

What is the benefit for a woman to get tested? Of the 1000 women who will be screened, only 1 will be saved in the best case (5 deaths - 4 deaths). If we express it in percentage, it gives therefore 1/1000 is 0.1% (much less attractive than 20%!)

The art of manipulating opinion

It is interesting to translate the relative risk of dying from breast cancer into more familiar situations. Thus, in his book "Thinking Risk" Gerd Gigerenzer notes:

"It can be said that having an annual screening mammogram, assuming a 25% decrease in relative risk, has about the same effects on life expectancy as reducing the distance traveled by car each year." 500 km. "

The art of manipulating opinion

On the other hand, the overall effect of screening on mortality is more complex than measured by the study of breast cancer specific mortality.

Breast cancer mortality is not counted for deaths caused by screening, due to surgical or anesthetic accidents, to the complications of chemotherapy and radiotherapy, such as cardiovascular and radiation-induced cancers.

Studying the overall mortality allows to include all the effects, expected and unexpected harmful, of screening. The benefit / risk ratio of screening is thus clearly unfavorable.

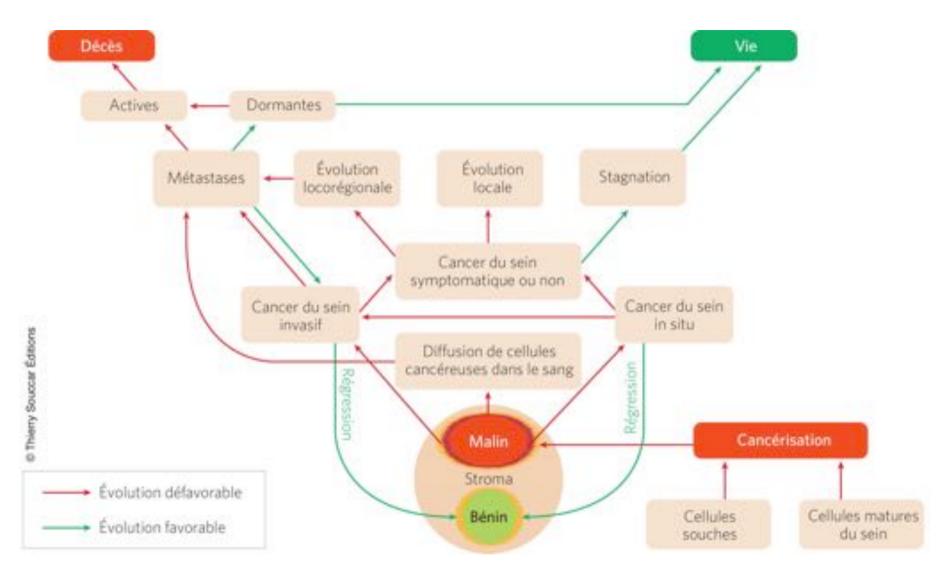
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The halstedian schema of the natural history of breast cancer is not the right one. The mechanical and linear evolution in time is contradicted by the facts. There is no unidirectional arrow leading inevitably to death.

Today, the only thing we know is that we do not know.

This should lead the medical profession to be more modest, to be less peremptory in its diagnostic and therapeutic indications and to stop excessive medicalization of healthy women on the pretext that they are potential patients.

Time is up for alternative hypotheses



The tumor is not only reduced to genomic alterations, it is also the product of interactions with the environment, which get entangled at all levels, leading to either continuity of life, regressions of anomalies or death. It's a bush of possibilities.

How to get out of the quagmire where mass screening has led women

- Before screening,
- answer the question "should I participate in screening? Is easy today.
- The question is posed in a climate of serenity by women in principle healthy.
- They can consult an abundant literature that shows that screening mammographic or selfexamination is both ineffective and deleterious.
- Downstream of screening,
- how to help women diagnosed with cancer?
- It is not known whether or not their cancer is overdiagnosed. As soon as cancer is diagnosed, medicine offers nothing else in the current context than to treat and possibly overtreat, taking the risk of major side effects (while new practices are ethically possible when the concept of overdiagnosis is recognized).
- To avoid admitting their failure, the promoters of screening claim improve it without questioning its legitimacy.
- Well, the more we improve the screening, the more it becomes perverse.
- The problem is not in form but in substance.

And if the energy deployed today in screening awareness campaigns was used in the effort of a new understanding of the disease ...

The disease has no need for rules that have been prescribed for more than a century by a medicine unable to answer the most basic questions:

- What is cancer, how to define it?
- Where is the deadly disease and where is the harmless that should not be detected?
- Being a carrier of cancer cells, from when are we sick?

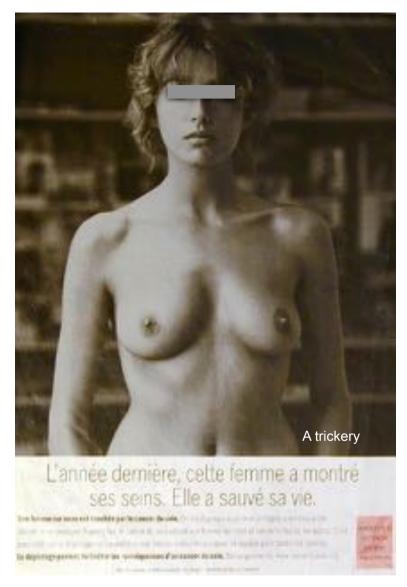
Three attitudes towards halstedian schema and overdiagnosis



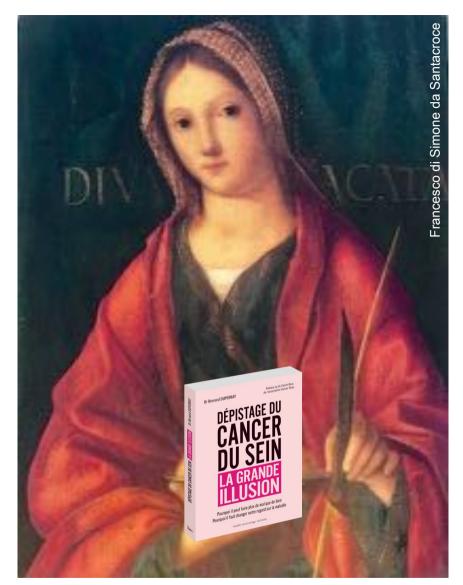




running away perplexity fight



In fact, we should say: this woman has shown her breasts, we confiscated her health, spoiled her life, changed her into a commodity because, in the best case:

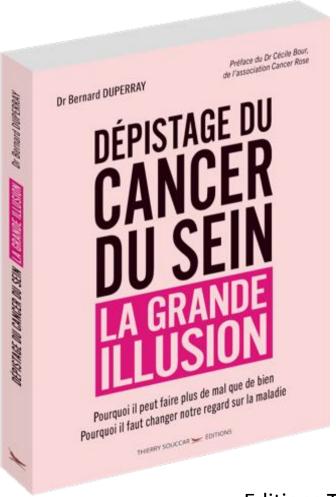


in 2000 women screened for 10 years:

- 1 will see her life lengthened.
- 10 will be treated unnecessarily and more than one will die as a result of her diagnosis.

200 will be worried by a false positive.

 The argument of this presentation is based on the bibliography of the book which includes 208 references.



Editions Thierry Souccar