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Probability revision in general practice: occult blood in stool in patients with indigestion, and daily smoking in patients with cough

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Eine korrigierte Wahrscheinlichkeitsberechnung in der Allgemeinpraxis: Okkultes Blut im Stuhl im Verhältnis zu Verdauungsstörungen und tägliches Rauchen bei Patienten, die husten

Zusammenfassung. Die frühere Berechnung den positiven Prädiktionswert eines Symptoms im Verhältnis zu einer Erkrankung und mit Einberechnung von Geschlecht und Alter, ergibt die Grundlage für die Wahrscheinlichkeitsberechnung bei neuen Informationen über Krankheitszeichen, die während eines Krankheitsverlaufes auftreten und in einer Sprechstunde beurteilt werden. Das Zeichen kann ein Symptom sein, eine Information aus der Krankheitsgeschichte, eine Entdeckung bei der Untersuchung, oder auch ein Labortestergebnis. Die Wahrscheinlichkeitsberechnung erfordert den Wert der Sensitivität und Spezifität des Krankheitszeichens. Die Wahrscheinlichkeitsberechnung mit folgenden positiven und negativen Zeichen ist hier für okkultes Blut im Stuhl im Verhältnis zum Colorectalkrebs bei Patienten mit Verdauungsstörungen in der Allgemeinpraxis gemacht worden, und auch für tägliches Rauchen im Verhältnis zum Lungenkrebs bei Patienten, die husten. Ein positiver Test für okkultes Blut im Stuhl gibt ungefähr eine fünffältige Erhöhung den PPV für alle Altersklassen. PPV übersteigt 10% für Patienten von 50 Jahren und älter, und ab 70 Jahren ist PPV 18,9% für Männer und 25,0% für Frauen. Selbst mit einem negativen Test für okkultes Blut im Stuhl verbleibt PPV ungefähr 1% für alte Patienten. Tägliches Rauchen bei 60–69jährigen Patienten, die husten, erhöht den PPV von 6,4% bis 8,5% bei Männern und von 0,8% bis 2,0% bei Frauen. Auch LR wird erhöht. Tägliches Rauchen ist viel üblicher als dauernder Husten und hat in sich selbst einen ganz geringen PPV für Lungenkrebs. Es wird gezeigt, daß ein Zeichen, das bedingt unabhängig von den Zeichen, die in der Berechnung der früheren Wahrscheinlichkeit benutzt werden, nützlicher ist als ein Zeichen, das nicht bedingt unabhängig für die untersuchen Patienten vermutet werden kann.

Summary. Prior calculation of the sex- and age-distributed positive predictive value (PPV) of a symptom in relation to a disease forms the basis for probability revision based on new information about signals observed during the medical encounter: a symptom, a sign, a piece of information based on the medical history, a laboratory test. Probability revision requires estimates of sensitivity and specificity of the signal. Probability revision following positive and negative signals have been made for occult blood in the stool in relation to colorectal cancer in patients presenting in general practice with indigestion, and for daily smoking in relation to lung cancer in general practice patients with coughs. A positive test for occult blood in the stool gives an approximately fivefold rise in PPV for all age groups. For patients 50 years of age and more PPV exceeds 10%, and for patients 70 years old or more PPV is 18.9% for men and 25.0% for women when the test is positive. As expected, the predicted value decreases when the test is negative, but for old persons the predicted value is about 1% even when the test is negative. Daily smoking in 60- to 69-year-old patients with coughs increases PPV from 6.4% to 8.5% for men, and from 0.8% to 2.0% for women. The likelihood ratio (LR) also rises. Daily smoking is much more common than coughing in the general population, and daily smoking in itself therefore has a lower PPV for lung cancer than a persistent cough. The change in probabilities after revision is illustrated. The results confirm that a signal conditionally independent of signals used in the calculation of prior probabilities is more useful than a signal that cannot be assumed to be conditionally independent for the patients studied.

A study of the seven warning signals of cancer in general practice in the municipality of Tromsø, Norway, has permitted calculation of positive predictive values (PPVs) for some important forms of cancer when patients present with such symptoms [1]. As

single symptoms, most warning signals are poor predictors of cancer. However, especially in high age groups, a PPV may be high enough to provide a strong incentive to carry out further investigations.

Decisions in general practice are mostly based on the combination of many small pieces of information or signals. Most signals become available by way of such simple, quick processes as asking questions, inspecting and palpating, or taking and analysing a blood sample. In major diseases such as cancer, the high technology found only in hospitals is often necessary for diagnostic conclusions. It is common for doctors to think that most of the signals encountered in general practice are of very limited diagnostic value. This is true to the extent that they are referred to a population in which most diseases have a very low prevalence. However, single signals in general practice can lead to major revisions of prior probabilities if the general practitioner is aware of two preconditions: prior probability should be increased by defining each patient in a hypothetical population of the same sex and age as the patient, sometimes with some other common characteristics as well, and for revision of this probability general practitioners should concentrate on signals that may be assumed conditionally independent [2] of previously applied signals in the relevant disease.

Materials and methods

Prior probabilities of cancer were calculated from three populations of cancer patients in Tromsø, and from a multipractice registration of warning signals at encounters in general practice in Tromsø [1]. Population statistics and official cancer statistics [3] are from the same year (1982) as the warning signal study.

For cancer of the colon, the sex- and age-distributed PPV in patients presenting with "indigestion or change in bowel habits if this is not rapidly normalized" (abbreviation: indigestion, or I in the tables) has been calculated. The likelihood ratio (LR; the probability of indigestion in patients with cancer of the colon divided by the probability of indigestion in patients without cancer of the colon) is also presented (Table 1). Corresponding probabilities for lung cancer in patients presenting with "hoarseness or coughing without any apparent reason" (abbreviation: Cough/hoarseness, or C, H in the tables) are presented in Table 2. In an earlier paper [1], the indexes were shown as a range of values based on a sensitivity range for the symptom as an indicator of cancer at the time of an encounter. In Tables 1 and 2 the indexes are based on a single median sensitivity estimate, which is 0.35 for indigestion and 0.25 for cough/hoarseness [1]. Another implicit assumption concerning the diagnostic indexes in Tables 1 and 2 is that the average period of possible diagnosis is somewhat shorter than 1 year, and that people with a diagnosable cancer visit their general practitioner more often than people without cancer [1]. This has been discussed in more detail elsewhere [1]. Some of the estimates behind the indexes may differ in other places and at other times. The values in Tables 1 and 2 should therefore be read only as approximate levels of probability given certain preconditions, as an illustration of the variation with sex and age and as a reference base for revised probabilities.

For a patient with indigestion, a search for occult blood in the stool (OBS) is commonly used. For a patient presenting with cough/hoarseness most doctors would want to know whether he or she was a daily smoker (DS). In both cases cancer would be among the diagnostic hypotheses considered by most general practitioners, even though new cases of cancer are quite uncommon in general practice. We shall consider the potential benefit of these two signals, one based on a simple laboratory test requiring some practical cooperation from the patient and the other on a simple question, in cancer diagnosis.

Table 1. Age distributed positive predictive value (PPV) and likelihood ratio (LR) of indigestion (I) in relation to cancer of the colon, including rectum (CC). (Modified from [1])

Age group	PPV (P ⟨CC/I⟩)		LR	
	Males	Females	Males	Females
20–29	<0.1%	–	27	–
30–39	0.1%	0.1%	25	27
40–49	0.5%	0.5%	23	25
50–59	2.2%	1.8%	36	30
60–69	2.3%	2.2%	16	16
70+	3.4%	4.8%	9	18
20+	2.0%	2.5%	26	33

P, Probability; ⟨X/Y⟩ = X given the presence of Y; sensitivity of indigestion presented during consultation (P ⟨I/CC⟩) = 0.35

Table 2. Age distributed PPV and LR of cough/hoarseness (C, H) in relation to cancer of trachea/bronchus/lung (LC). (Modified from [1])

Age group	PPV (P ⟨LC/C, H⟩)		LR	
	Males	Females	Males	Females
20–29	–	–	–	–
30–39	–	0.1%	–	42
40–49	–	0.2%	–	36
50–59	–	0.8%	–	28
60–69	6.4%	0.8%	38	21
70+	–	1.1%	–	25
20+	9.0%	0.8%	137	42

P, Probability; ⟨X/Y⟩ = X given the presence of Y; sensitivity of cough/hoarseness presented at an encounter (P ⟨C, H/LC⟩) = 0.25

Modern tests for OBS, when correctly used, usually have a sensitivity around or above 80% for detecting colorectal cancer [4]. A Norwegian screening study [5] permits a rough estimate of around 88% for test specificity. Faecal blood was demonstrated in 50 of the 413 patients who returned faecal samples, who for present purposes are assumed to be representative for the statistically selected total number of 754 persons approached. One colonic carcinoma was found, about as expected in this population of 54- to 64-year-olds [5]. In our calculations a sensitivity of 80% and a specificity of 88% have been used for all age groups. Colonic cancers may cause occult bleeding without giving rise to indigestion, and indigestion may probably be present even if no occult bleeding can be detected. It seems reasonable to assume that the presence or absence of indigestion and the result of the test are conditionally independent for our cancer patients. Probability revision for cancer has been made for both sexes and for different age groups of patients presenting with indigestion, for both positive and negative tests. The pitfall of negative tests for OBS in cases of colonic cancer is only too well known to many general practitioners.

For lung cancer the probability revision has been limited to patients 60–69 years old. For other age groups there were too few records of cough/hoarseness in men to permit calculations of PPVs. For women, PPVs for lung cancer in patients with cough/hoarseness in 1982 were low in all age groups. These probabilities have proba-

Table 3. Probability revision for cancer of the colon (CC) in a patient presenting with indigestion (I): usefulness of a test for occult blood in stool (OBS)

Age group	P⟨CC/I and OBS+⟩		P ⟨CC/I and OBS−⟩	
	Males	Females	Males	Females
20–29	–	–	–	–
30–39	0.7%	0.7%	–	–
40–49	3.3%	3.3%	0.1%	0.1%
50–59	13.3%	10.6%	0.5%	0.5%
60–69	13.3%	13.3%	0.6%	0.5%
70+	18.9%	25.0%	0.8%	1.2%

P, Probability; ⟨X/Y⟩ = X given the presence of Y; sensitivity of signal (test) = 80%, specificity = 88%

Table 4. Probability revision for lung cancer (LC) in a patient presenting cough/hoarseness (C, H): usefulness of information about smoking habits (daily smoking = DS) in the age group 60–69 years

	Males		Females	
	P	LR	P	LR
P ⟨LC/C, H⟩, and LR	6.4%	38	0.8%	21
P ⟨LC/C, H and DS⟩, and LR	8.5%	52	2.0%	50
P ⟨LC/C, H and no DS⟩, and LR	3.3%	19	0.3%	8
P ⟨LC/DS⟩, and LR	0.4%	2	0.1%	3

P, Probability; ⟨X/Y⟩ = X given the presence of Y; sensitivity of signal (DS) in LC patients: 80% (males), 70% (females); Frequency of DS in the general population of 60 to 69-year-olds: 40% (males), 23% (females); Frequency of DS among patients 60 to 69-years-old who consult for cough/hoarseness: 60% (males), 30% (females)

bly increased since 1982 because more women smoke, and the incidence of lung cancer in women is on the increase.

In 1982 approximately 40% of Norwegian males and between 20% and 25% of females in the age group 60–69 years were daily smokers [6]. However, it seems reasonable to assume that a larger proportion of smokers than non-smokers acquire coughs leading to a consultation. We cannot assume conditional independence for cough and daily smoking in lung cancer patients. In the probability revision I have assumed that 60% rather than 40% of the 60- to 69-year-old men consulting for cough/hoarseness smoke, and 30%, rather than 20–25% of women. About 80–90% of males with lung cancer smoke; the corresponding percentage is lower in women [7]. For calculation purposes I have used 80% as the figure for daily smokers among male lung cancer patients 60–69 years old, and 70% for daily smokers among women in the same age group.

Revision of prior probability was calculated from a 2×2 contingency table [2]. Identical results are obtained through the alternative methods of substituting probabilities directly into Bayes' formula or through inverted probability trees [2].

Results

The revised probabilities are shown in Tables 3 and 4. In Table 4 likelihood ratios (LRs) for single and combined signals in relation to lung cancer are included.

Apparently very important information is obtained through the test for OBS in patients 50 years of age and older. It is also confirmed that cancer of the colon is not impossible even when no blood is detected in the stool.

The increase in the probability of lung cancer for daily smokers is less impressive, although there is a clear difference in the probability of lung cancer between smokers and non-smokers. The LR is much higher for cough/hoarseness alone than for daily smoking alone, implying that cough/hoarseness is a better discriminator of lung cancer than daily smoking.

Discussion

Local values should be based on local estimates of prior probabilities, and extrapolation of the numerical values to other situations is not possible. The change in probabilities after revision is nicely illustrated.

In persons more than 50 years of age the probability of cancer of the colon (or other parts of the gastrointestinal tract), given indigestion and a positive test for OBS (Table 3) is strikingly high compared with the modest prior probabilities in Table 1. The test, given that our assumption about conditional independence of previous information is correct, has made possible a probability revision sufficiently important to have practical consequences. It is of course possible that the assumption of conditional independence is wrong. Perhaps colonic cancers causing indigestion have a greater tendency to bleed than when there is no indigestion. In that case the probability change would be less important. If we trust our assumption, the calculations give a good rational background for referral for endoscopic or other specialized investigations. An ordinary clinical examination, including rectal examination, is of course performed when the patient originally presents with indigestion, but it seems superfluous and a waste of time to wait for the results of additional tests.

In persons below 50 years of age it would be much more justified to repeat the test for OBS, complete the medical history and the clinical examination in the general practitioner's own office, carry out supplementary tests and observe the development of the symptoms before deciding about referral to specialists. There is no justification for letting the patient go without making a further appointment for monitoring; a 1–5% probability of a potentially dangerous and often curable disease such as cancer of the colon necessitates further investigation in some way or another. This also tells us to consider further investigation in an old person with a negative test for OBS when indigestion is present. The probability of cancer of the colon is as high in a patient over 70 with a negative test as in a 30- to 39-year-old with a positive test for OBS. The probability of cancer of the colon is very low in persons less than 50 years old when there is no OBS. Consideration of the patient's age is essential, while

the patient's sex is of less importance in this disease, which has similar although not equal incidence rates for males and females in the different age groups.

The value of information about smoking is reduced when it is considered together with a smoking-dependent symptom like cough/hoarseness. The difference in LR (Table 4) reflects the fact that daily smoking is much more common among 60- to 69-year-olds than is any point prevalence of cough/hoarseness. Therefore daily smoking is only twice as common in a population of 60- to 69-year-old men with lung cancer than in a similar population without lung cancer. Even though cough/hoarseness is a much better discriminator of lung cancer, we need additional information such as information on daily smoking, because the probability of lung cancer, given cough/hoarseness, is rather low, especially in women. Without the information about smoking it might seem justified to order a chest X-ray of all male but no female patients with cough/hoarseness in this age group. For male smokers this attitude is only slightly strengthened by the new information. For non-smoking males it becomes easier to defend a postponement of any decision about chest X-ray. To justify a chest X-ray for a woman or for a man who does not smoke we should probably possess more clinical information, increasing the probability of cancer and thus strengthening the basis for our decision.

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Buchbesprechungen

Meinert, C. L.: Clinical Trials – Design, Conduct and Analysis. New York, Oxford: Oxford University Press 1986. 469 p. ISBN 0-19-503568-2

Having been edited in the "Monographs in Epidemiology and Biostatistics"-series of Oxford University Press this book offers profound basics on how to design, conduct and analyze clinical trials. Being widely neglected during medical studies and continuous formation, the methods of clinical trials have become the most important way to prove effectiveness of treatment in today's medicine. The contents start with general deliberations on a trial to be designed (i.e. multicenter versus single-center trials, coordination, costs) to give most important hints on essential design features in the second part of the book. Sample size and power estimates, randomization, study plans and data collection considerations are being discussed. Furthermore, for execution, data analysis and interpretation important tools are being shown. Wide space is dedicated to management, administration and reporting procedures on clinical trials. Where is the importance of such a book for general medicine? I think there are at least two reasons for dedicating some time to its lecture. First, we all accept new notions on medical practice deriving from such trials. Hence the necessity to be able to judge on their quality and impact for daily practice. Second, if general medicine wants to develop own skills on conducting trials in private practice, this book offers a wide range of methodological basics to know and to adapt to the circumstances of general medicine. This does not mean that a general practitioner should be able to perform statistical circulations on its own after studying thoroughly a book like this. But I think we need to gain some basic knowledge on biometrics to be able to contribute in a team designing, performing and analyzing trials in general practice.

M. Kirchgeorg, München

W. Ulmer et al.: Husten – Ätiologie, Pathophysiologie, Klinik, Differentialdiagnose, Epidemiologie, Therapie. Stuttgart: Kohlhammer 1987. 192 S., 2 Fotos, 46 Abb., 15 Tab., Pappbd., DM 39,80. ISBN 3-17-009803-9

Fast 200 Seiten über Husten – jeder praktisch tätige Arzt wird nützliche, bisher unbekannte Aspekte in diesem Buch entdecken. Die Verfasser – Mitglieder einer Arbeitsgemeinschaft der Universität Bochum – stellen die (Patho)physiologie des Hustens und die (differential-) diagnostischen Möglichkeiten gründlich dar, sind aber erkennbar bemüht, kein pneumologisches Lehrbuch zu schreiben, sondern beim klinischen Thema zu bleiben. Daten über das allgemeinmedizinische Präsentieranliegen „Husten" fehlen dennoch, ebenso eine kritische Bewertung der Vielzahl diagnostischer Methoden nach Kriterien der Testgüte, der therapeutischen Relevanz und gesundheitsökonomischen Aspekten. Auch das therapeutische Arsenal verdient eine Hervorhebung von Einsparpotential. Eine 2. Auflage ist zu wünschen.

B.-P. Robra, Hannover