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Forty Years of Arctic Primary Care Research on the Early Diagnosis of Cancer

Knut Holtedah

Abstract

Usually, before a patient with cancer can be treated in a hospital, a general practitioner (GP) must suspect the diagnosis and refer the patient. GPs often worry that they could have done better for some of their cancer patients. Had there been an unreasonable delay of diagnosis? In the arctic, rural/urban city of Tromsø, this question became the subject of several scientific articles. Symptoms was an evident gateway to thinking about cancer in patients. In later years, there has been an explosion of good research studies about early diagnosis both in primary and secondary care. Through a northern gaze, the reader will be guided through a journey covering forty years of primary care-based research aiming at earlier diagnosis of cancer. Summing up, suggestions are given for: How to react upon signals from the body? And for the GP: 1. Explain unusual symptoms. 2. Add results from clinical findings and testing to symptoms. 3. Refer when the probability based on symptoms and findings exceed 3%. 4. Consider 'fast track' when you seriously suspect cancer. 5. Think of early diagnosis of cancer as an important, challenging and interesting part of your effort to serve the patients who consult you!

Keywords: Neoplasm, Oncology, Early diagnosis, Primary care, General practice, Family practice, Public Health

1. Introduction

Care for people with cancer: the task is universal, but conditions vary in different areas of the world. Tromsø, in the beginning of the 1970s, was a small city with a recently established university, the northernmost university in the world. The oncological department was yet to come, and surgeons and internists dealt with patients in collaboration with oncologists in the bigger, southern cities.

Then there were the general practitioners (GPs). In the homes, some of the patients were ill with cancer. Time to talk, some relief, morphine for pain, and repeated visits, this was enriching for the GP and sometimes comforting for the patient and the family. Tromsø covered a large, arctic island community, part urban and part rural, with closeness to sea and mountains, where summer brings the midnight sun and winter features northern light and pastel colours and snow. For a GP, home visits were many, always on duty nights, and sometimes also on ordinary working days to patients calling the surgery. Means of transport, on sunny days and through winter wind and snow, were private cars, but also all kinds and

sizes of boats and exceptionally a seaplane or a helicopter. Occasionally, medical things were put in a rucksack in order to go skiing to the patient – a mode of home visit that was more common and over greater distances in the previous generation of GPs. Many Norwegian GPs would recognise descriptions and photos in Berger & Mohr's beautiful book about a fortunate man [1]. The book follows an English rural GP, dedicated to his practice and his patients, trying to combine empathy and lessons from life with wide-ranging theoretical learning that can help his patients. Landscapes may differ, but the GP's tasks were much the same.

In these homes, as well as in the surgeries, many questions came to mind. This article will concentrate on a question which arose naturally in this primary care context: Can cancer be diagnosed earlier? Many researchers have contributed to the present-day knowledge and understanding. Some early studies were performed in Tromsø. They may be a suitable starting point for a somewhat personal story about the modern development of early diagnosis primary care research. Altogether, in 2021, there are some answers to the question.

2. Early diagnosis of cancer, in primary care

GPs see some patients requiring urgent hospitalisation, turning out to have incurable cancer. Often, GPs will ask themselves whether they have reacted reasonably quickly to worries and symptoms presented? Could something have been done better? What about the young woman with a seemingly innocent lump on her neck, turning out to be an oral cancer? Or the man with long-standing abdominal pain who got a follow-up appointment but never returned? He died from a stomach cancer. An elderly woman got antibiotics twice after delivering bloody urine specimen to our lab. The third time, she was contacted and asked to come for an appointment, and yes, the blood came from a cervical cancer.

GPs benefit from much trust. People expect their GP to understand and react professionally, without delaying a diagnosis like cancer and the time before treatment may start. A patient seen by an oncologist or a surgeon would commonly be rapidly diagnosed. However, how would the specialist know about that patient if the GP did not refer, or only did so after the cancer had spread?

3. Why writing now?

Hopefully, senior medical students and young doctors in vocational training could learn something useful from this story. Younger GPs -including GPs working in rural areas where they often know their patients well – might become more confident in their clinical practice, and some might open to the possibility of transforming good questions into research. Contributing to the knowledge base is important for the exercise of medicine. Some of this knowledge should be produced in primary care, in order to get the whole picture of diagnostic challenges. Primary care must be an integrated part of the research community.

Finally, it would be nice if some readers think they get a better idea about when to see their GP if the thought of cancer bothers them, and about what to expect from the GP. The language here is simple enough for lay people to follow.

As this story develops, some results have been quoted and short commentaries given. For detailed methodologies and more extensive discussions, the reader may consult the articles in the literature list.

4. The leap into research: 1977-1984

In Norwegian medical schools, general practice was not taught as a specific topic until around 1970. General practice was not among the more prestigious disciplines in medicine, and GPs were not frequently authors of scientific papers.

Still, most students graduating from medical schools found work in general practice. During the 1950s and 60s, some brave British GPs like John Fry and John Howie ventured into more systematic studies. Even before them, the productive Robert Braun in Austria had made diagnostic checklists for general practice. In Norway, Bent Bentsen gathered practice registration material in his own surgery [2].

At this time, academic departments of general practice appeared in several countries, introducing relevant student teaching and new research agendas. A formal specialty of general practice was acknowledged in more and more countries.

One interesting initiative occurred in Norway: The national medical association decided to encourage this revival and financed the first professorship in general practice in Oslo. And: They gave practice compensation payment for up to six months for GPs wanting to take a research leave after presentation of a project.

This encouragement resulted in a project description and an application from Tromsø. Did some cancer patients have their diagnosis delayed by incorrect handling in primary care? A friendly librarian at the University library searched their recently acquired databases for articles combining keywords 'cancer' and 'general practice'. Articles were found, saying for instance that an early diagnosis was often important for patient prognosis [3, 4]. And there it was, the word matching many previous thoughts: DELAY. Diagnostic delay. Somebody had been interested in this, and had written about it [5, 6], a couple of them in general practice [7, 8]!

5. Delay

All GPs in Tromsø agreed to find medical journals for patients diagnosed with cancer, and one GP researcher went through all journals, taking structured notes. On request, the Norwegian Cancer registry furnished a list of all 108 patients in Tromsø municipality having been diagnosed with cancer in 1976. The following was noted from the medical journals: Age, sex, civil state, rural/urban habitat, weeks from first symptom to first consultation, weeks from first consultation to diagnosis. Also, laboratory tests and X-rays taken the last year, and an admittedly subjective but criteria-based evaluation of what seemed like reasonable actions for that type of cancer, in the situations described in the journals. Did the medical history appear sparse, adequate, penetrating? Was the clinical examination insufficient, good local/regional, or extensive? Did the researcher think there was diagnostic delay, based on the conclusion in the medical journal notes, the type of cancer and the number of weeks noted for the two intervals examined? If so, was this due to what the patient did, or to what the GP did? Given the conclusion the GP described at the end of the consultation, did the researcher think that the GP could have done a better job there and then, and thereby reduced a possible delay?

The University hospital also gave access to their archives. The same kind of anonymous structured notes were taken from their machine written journals, altogether 25 archives from primary or secondary care, for a population of 45000 inhabitants.

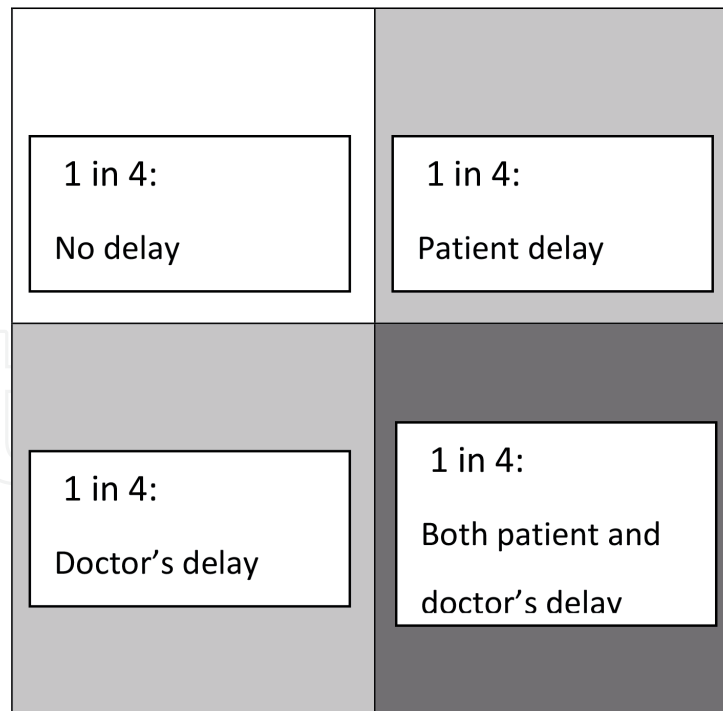


Figure 1.
Diagnostic delay of cancer in medical journal study, 108 patients in Tromsø, Norway, 1976.

5.1 Results

Three quarters of the patients could have had their diagnosis made earlier: Half of all patients saw their GP rather late in the course of the disease. In half of the cases the GP or the hospital doctor could have improved the diagnostic work-up. The overlap left one fourth of all patients with no kind of delay. Long waiting lists in primary or secondary care also played a part. (**Figure 1**).

What could have been done better? For 43 of the 108 patients, one or more of these were noted: Apparently no follow-up when needed, insufficient medical history, insufficient clinical examination, lack of relevant laboratory examination or of x-ray referral, no or late referral to secondary care.

5.2 Short reflection

What was lacking, was good old GP work, with a potential of improvement through vocational training and continuous education!

6. Symptoms: seven warning signals of cancer

Symptoms patients had presented at consultation, also were recorded from the medical journals. Medical journals are not reliable sources of everything going on in a consultation, but symptoms seem to be among the well documented topics [9]. Many symptoms had been noted in medical journals from both primary and secondary care.

At that time, in most patient waiting rooms, there were posters quoting ‘Seven warning signals of cancer’ (**Table 1**). The posters advised patients to tell their doctor if they experienced any such symptoms. The first mention of ‘the danger signals of cancer’ occurred in a pamphlet developed during World War I, in a desire to

Seven 'classical' warning signals of cancer

1. Any sore which does not heal
2. Lumps anywhere in the body, especially in the breasts, and even if they are painless
3. Abnormal bleeding from body orifices
4. Changes in colour or size of warts or moles
5. Indigestion or change in bowel habits, if this is not rapidly normalised
6. Hoarseness or coughing without any apparent reason
7. Weight loss without any apparent reason

Abbreviations used in text:

1. Sore
 2. Lump
 3. Bleeding
 4. Mole
 5. Indigestion
 6. Cough/hoarseness
 7. Weight loss
-

Table 1.
Seven 'classical' warning signals of cancer.

stretch medical resources and to emphasise disease prevention. Three such signals were soon distributed to the public, and by 1929 they had been translated into 22 different languages, despite no scientific studies validating the signals. By 1951, the number of signals had increased to seven (Personal communication, Gerry de Harven, American Cancer Society). By 1982, 'danger signals' had changed names to 'warning signals', and a minor revision made the first letter in each signal form the word CAUTION. The Norwegian translation was a quite accurate translation from the American original.

6.1 Results

One or more of the seven symptoms had been presented by 68 of the 108 patients with cancer. However, 35 patients presented other symptoms, a quite varied list. Most symptoms, including those on the list, were common and it could only be assumed whether the symptom stemmed from the cancer. Still, with a known cancer location, many recorded symptoms seemed to fit with the diagnosis. Some symptoms seemed to be better known than others by the public: lumps and irregular bleeding more quickly than other symptoms led to GP consultations. Overall, non-warning symptoms did not lead to slower consultation than warning signals.

6.2 Short reflection

It was possible that the list had a mission in reminding the GPs of being vigilant. The public may be more aware of some symptoms than of others. The role of warning signals seemed to merit further studies.

7. Publish!

The Journal of the Norwegian Medical Association published this study. A first article detailed the background, method, results and conclusions, and a second article gave casuistic examples of what the GP might improve [10, 11].

By now, a regular contact at the university library had been established. What had been written previously about early cancer diagnosis, was eagerly studied. In a British article from 1966, Grey [12] described how cancer can bring patients to GPs and the possible reactions of the doctor. Whole person medicine is the GP's starting point in consultations. From there, the medical history, the clinical examination and various tests and referral possibilities is the way to go. Patient delay, GP delay, hospital delay and even government delay from insufficient financing of health services, were described with casuistic examples.

Patient delay had been discussed considering social psychological factors in two articles from the US [13, 14]. Some hospital based articles described delay in relation to specific forms of cancer [15]. Jenkins' article on delay and Macadam's article focusing on gastrointestinal cancer were contemporary investigations from general practice [16, 17].

New questions were triggered by the original study. How frequent were the warning symptoms among patients consulting in general practice? - according to GP registrations, and according to patients interviewed after their consultation? In a general population? Had newly diagnosed cancer patients consulted for warning signals more often than other GP patients? Over the next three years, these questions were studied with a basis in general practice in Tromsø.

8. Warning signals in patients who consult

Fourteen GPs from four group practices, almost all GPs in Tromsø, registered anonymously for six months consecutive patients on an A6 card immediately after the consultation, marking initials, sex and date of birth. A cross in a square, one for each symptom, identified patients who presented one or more of the seven warning signals.

8.1 Results

In 11606 patients, 649 symptoms were recorded. Three of the signals, 'lump', 'bleeding' and 'indigestion' (**Table 1**) occurred far more often than the other signals. On average, warning signals were presented in 5.4% of all consultations, more frequently in women than in men. This was expected because of the possibility of lumps in breasts. The rate of warning signals increased with age, except for 'lump' which was frequent in children and young persons, and 'bleeding', frequent in younger women.

8.2 Short reflection

At that time, Norwegian GPs saw approximately 20 patients a day. If one in twenty patients presents a warning signal of cancer, it meant that on average, one such patient would consult a GP every day. That did not mean that many of them had cancer, but it meant that GPs had to think of that possibility at least once most of our working days!

9. Warning signals in the general population

The posters in waiting rooms and in the municipal bus aimed at informing patients and the general population. The symptoms should initiate a visit at their GP's surgery. How frequent were these symptoms? Did people really go see their doctor?

Two medical students in Tromsø volunteered to do a door-to-door survey in two areas of Tromsø, one with small houses and many elderly inhabitants, and one with a more suburban mix of higher concrete buildings and rows of houses. Every other entrance or house were visited in early evenings by one or the other student. Local papers had informed about the study. The presentation procedure and questioning had been standardised. People who consented to participate, were asked whether they during the last three months had experienced any of the seven symptoms which were read to them one by one. The A6 cards from the consultation study served to record the answers.

Moreover, one of the students was engaged to sit for one day at the waiting room of each of the four group practices while the consultation study was being done. When a patient came out of a GP's office, the students would ask for a brief interview and record symptoms the patient thought they had presented to the doctor. The answers were compared to the GP's registration for the same consultation.

9.1 Results

In 299 persons from the general population, one fourth said they sometimes during the last three months had felt one of the symptoms read aloud to them. There was no difference between age groups. Half of these people had visited the GP for this reason, more so in the highest age group. These were higher proportions than what used to be found in studies about why people see a doctor [18], suggesting that the warning signals do promote visits to the GP. 'Indigestion', 'lump' and 'cough/hoarseness' were frequent. During the four interview-days in the surgeries, more patients than GPs thought that the patient had presented this kind of symptoms, 28% versus 10%.

9.2 Short reflection

The symptoms in question no doubt are present in people's mind, far more frequently than when they signify cancer. Increased consultation may become a burden for the health services; on the other hand, the symptoms have been shown to be relevant for cancer, and an increased tendency for consultation may be a good thing when cancer can cause the symptom. The GPs seem to have stricter criteria for recognising warning signals than people consulting them.

10. The first control groups: case-control study

If you investigate a group of patients, it is difficult to have a clear idea of what caused or expressed disease without a similarly constituted control group. The consultation registrations took place during six months in 1981-1982. A new retrospective study of medical journals was planned. For these six months, the Norwegian cancer registry again furnished a list of patients diagnosed with new cancer in Tromsø. For each of the 65 cancer patients, a control patient was found among the group of patients having consulted before any diagnosis of cancer had been made in

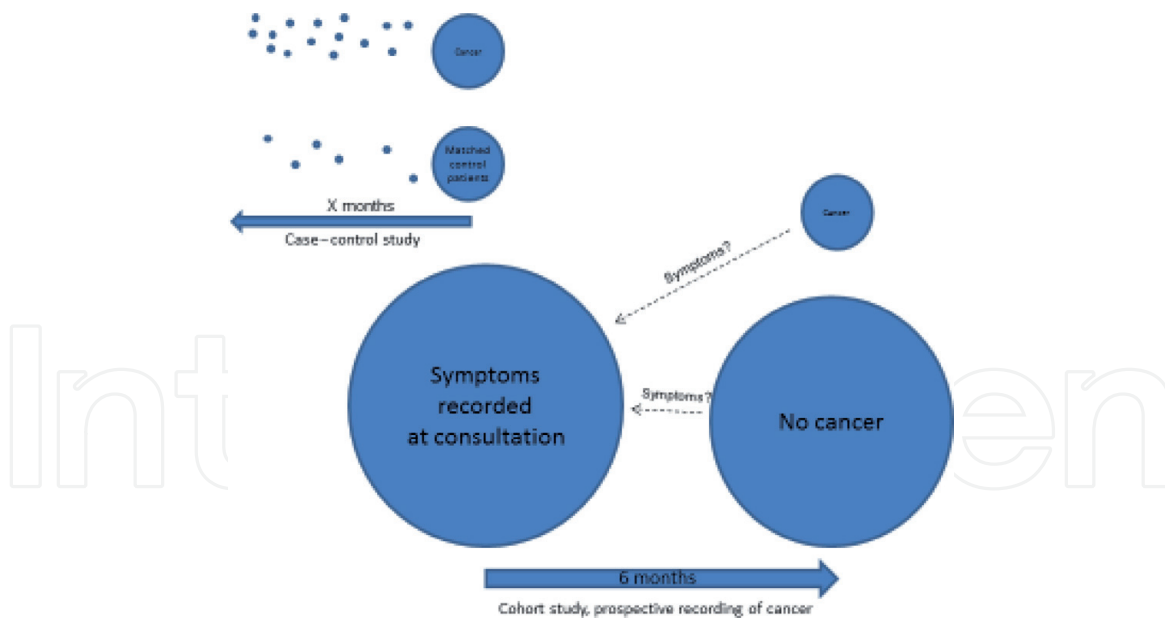


Figure 2.

Two kinds of study design: case-control study (looking back in time), and Cohort study with prospective recording of cancer (looking forward).

the cohort (**Figure 2**). Matching criteria were same sex and the closest possible date of birth. This time, criteria were made for early versus late symptoms in the cancer patients, to see the potential prognostic gain from early diagnosis.

10.1 Results

Two third of cancer patients had presented early warning signals, and about 35% of control patients had presented corresponding symptoms. The difference was statistically significant both for males and females.

10.2 Short reflection

When early warning signals are more frequent in cancer patients than in other consulting patients, a window of diagnostic opportunity exists for GPs.

Altogether five articles were now sent to the Norwegian medical journal [19], including a discussion of the content of the list of warning signals, and possibilities given by observations of the person-related data. Also, some more common diagnostic traps facing the GPs were discussed (**Table 2**).

Later, a list of Tromsø cancer patients diagnosed during the first eighteen months after the symptom registrations, was provided by the Cancer registry. Eighty of these cancer patients could be found among the recorded consulting patients. A new matching with 80 control patients based on the same criteria as in the previous study, was performed. Additionally, three GPs performed an inter-observer agreement study concerning what warning signals were found by each of them in the medical records.

10.3 Results

Warning signals were registered from the journals of 78% of cancer patients, before patient or doctor knew that the patient would get a cancer diagnosis, and in 26% of control patients. Again, this was a significant difference. Warning signals recorded only at consultation occurred in 20 cancer patients and 13 control patients. This difference did not reach statistical significance [20]. Agreement about the presence of warning signals in the journals, measured with kappa statistics, was

Traps for GPs in early diagnosis of cancer

1. GP does not follow-up positive findings
 2. Two most common clinical omissions: rectal examination, and not taking seriously what a woman feels in her breast if GP cannot confirm
 3. Early diagnostic hypothesis may be wrong
 4. Trauma in history is too easily accepted as an explanation for present symptom
 5. Comorbid benign disease is too easily taken as an explanation for present symptom
 6. Not all cancers produce the most common symptom; GP may sometimes repeat negative test
 7. If symptoms are diffuse, consider exploring deeper in medical history
 8. If symptoms are confusing, consider hormonal explanation – and if hormonal, consider cancer
-

Table 2.

Traps for GPs in early diagnosis of cancer.

good both for cancer patients and control patients, with some variation between different symptoms and less good in control patients [21].

10.4 Short reflection

The greater frequency of warning signals in cancer patients, found in the retrospective medical journal study, was not evident in the prospective recording of cancer patients. However, the tendency was in the same direction. Overall, based on all the studies, a majority of cancer patients experienced a cancer-related symptom which was communicated to a doctor some time before diagnosis. Furthermore, it seemed possible to rely quite well on registrations of symptoms from medical journals.

11. Strengthening the academic basis in the north: 1984–1991

During the 1980s, the topic of early diagnosis gained visibility in vocational training – in the North, and soon nationally. A GP colleague in Oslo started a PhD thesis in the same cancer field [22] and initiated a book about different cancer topics for GPs [23]. The next couple of years, GPs attended continuing education seminars and studied books that gave better insight in clinical epidemiology [24] and statistics [25]. Based on the investigations in the north, a thesis [26] and a practical manual for GPs [27] were written. The Arctic University had a Department of Community medicine, led by a GP professor, and several GPs started teaching and research in combined academic and clinical positions.

At this time, a big step in technology also created important changes: The typewriter had previously necessitated total re-writing of manuscripts needing changes. Now, the two-diskette-slot personal computer had appeared and developed into a movable computer with a 20-megabyte hard-disk and one diskette slot, opening a new world of free writing that could easily be corrected again and again.

12. A theoretical basis: understanding how probabilities may change

It had become quite certain that the probability of diagnosing cancer in a patient presenting a warning signal, was greater than in a patient without such symptoms.

However, with the many non-cancer patients presenting similar symptoms, it was clear that the probability of cancer was still very low. In order to refer a patient, a GP should be able to convince specialists that investigations in hospital would have a reasonable chance of revealing a cancer, preferably an early-stage cancer. Working with the Tromsø data, it was calculated how many of the patients with one or more warning signals had turned out to have cancer: this proportion, known to GPs as the *positive predictive value* (PPV), was 3.7%. Perhaps not very impressive in a referral letter, but we will get back to this figure.

A chapter in a book about decision analysis showed how the 18th century Bayesian thinking allow to update the probabilities of a hypothesis when evidence is added [28]. This is the way a GP works! The patient presents a symptom. The GP already knows something about the patient: age, sex, perhaps something about heredity and profession. Then the GP starts to explore the problem: a further medical history, a focused clinical examination. Cumulated additional information may allow upgrading the probability of cancer, or in many cases, dismiss such a hypothesis without bothering the patient or the specialist or the system with unnecessary procedures. The new information may not be independent of what we already know, but the GP may then apply Bayes' axioms of conditional probability to arrive at a reasonable update of the previous probability.

Three more articles resulted: two were about diagnostic indexes allowing quantitative judgement about the relationship between symptoms and cancer [29, 30]. The third article gave examples of revising probabilities of cancer: Based on data from the 1982 study, positive predictive value (PPV) was calculated from consultation data and then revised adding new information from the medical journals [31]:

12.1 Results/examples

A 60–69 years-old male with 'indigestion' had a PPV of 2.3% for colorectal cancer. Adding information about a positive test for occult blood, PPV rose to 13.3%.

A 60–69 years-old male with 'cough/hoarseness' had a PPV of 6.4% for lung cancer. Adding the information that this man was a daily smoker, PPV increased to 8.5%. If the man was a non-smoker, PPV decreased to 3.3%. The increase is smaller than for the occult blood example. This is because it may be assumed that 'indigestion' and occult bleeding are independent of each other, while 'cough/hoarseness' and daily smoking are less independent.

12.2 Short reflection

Such indexes can be calculated on the basis of empirical data. However, they also fit well with the more approximate way a GP works when analysing a patient problem. It is a way of thinking that implies both quantitative and qualitative considerations, and which most GPs apply intuitively and approximatively.

It is nice to be able to give examples based on data collected in primary care. However, we were still only in 1990 when these articles were published. Registrations in databases like Medline were in its infancy. The scientific journal, owned by Springer Verlag, ceased to appear the year after, and the articles in "Allgemeinmedizin" are not searchable in current databases. If you want to read the articles, you may use the Arctic University web-link given in the references. Also, for this and other examples of older articles in the reference list, a university library may help.

13. Academia: on the right track, with mixed feelings of enthusiasm and professional loneliness: 1992–1999

After rich years of full-time general practice, teaching and research at the university became a full time task for this author, although still with one day a week in the group practice in general practice. The 1990s was a period of increasing activity in primary care reunions, nationally and internationally, and many doctors presented primary care-based research. In some seminars and workshops, colleagues were asked to bring a cancer case of their own to discuss in small groups. This was motivating for the participants, who soon eagerly discussed how to improve their early diagnosis of cancer. Such group work later became part of the compulsory program in vocational training for the specialty of general practice in Norway. However, not everything was easy. The Arctic university was a young university, which admitted its first medical students in 1973. For the first decades, the competition for research grants was difficult with limited earmarking for primary care and competition with the more established universities. When grants were obtained, applicants for research positions were few. It was difficult to tempt colleagues living in the more populated south of Norway to apply for positions in the beautiful, but longer-winter north.

However, international primary care publications dealing with the early diagnosis of cancer, were relatively few during the 1990s. In workshops and congresses for GPs, interest in the subject was vivid, but with some exceptions [32, 33], the interest was only modestly reflected in studies from general practice. The focus on the early diagnosis topic weakened for a while at our department. General practice is a good place to get research ideas and produce evidence about many different clinical questions [34].

14. The times they are a-changin' – fortunately: research boost and Ca-PRI - from year 2000 and onward

Soon, however, a remarkable change occurred: Some GP based researchers, especially in the UK, but also in Denmark, Sweden, Belgium, the Netherlands, Australia, published interesting studies about the early diagnosis of cancer. They often drew upon large number of patients found in GP based databases and in official registries, and focused on major types of cancer [35, 36], in addition to cancer in general [37–40]. A GP can never know what kind of cancer the next patient presents, and it is useful to be prepared to diagnose just any cancer, frequent or rare. However, the frequent ones are more frequent and merit a closer look.

At this time in the north, all the almost 4000 GPs in Norway were invited to participate in an audit-type, one-sheet questionnaire study with much of the same intent as in previous studies, but this time recording cancer prospectively after an initial symptom registration in consecutive GP patients [41] (Cohort study, **Figure 2**). About 10% of the invited GPs volunteered to take part. In these studies, cancer suspicion was examined more closely.

14.1 Results

GPs' correct cancer suspicions were found to be six times more frequent than their erroneous lack of suspicion. Patient comorbidity and multiple consultations seemed to be underestimated by GPs as factors associated with cancer.

The discussion dealt with how GPs in their diagnostic attentiveness could consider ways of thinking, interpersonal awareness and relevant information related to symptoms and other factors [42]. The study also showed how a comprehensive GP approach should include knowledge derived from clinical examination and test results. This could increase sensitivity, i.e. findings correctly identifying patients with cancer, and help correctly suspect a diagnosis of cancer, in some cases with ‘low-risk-but-not-no-risk’ symptoms, or even without any relevant symptom [43].

14.2 Short reflection

The study suggests how knowledgeable, empathic medical work in primary care can make a positive difference for early cancer diagnostics.

Also, Johansen [44] interviewed GPs about the essential question “How does the thought of cancer arise in a general practice consultation?”

14.3 Results

Several contexts of attention were found: Practising basic knowledge, interpersonal awareness, intuitive knowing and fear of cancer. Such fear could affect both patient and doctor. Intuitive knowing was described as a tacit feeling of alarm which could be difficult to verbalise, but nevertheless was helpful. Intuition was supposed to build on the three other elements: knowledge, awareness, fear.

14.4 Short reflection

The complex quality of diagnostic analysis is demonstrated here through a qualitative approach. The study was performed around the same time as the previous, quantitative study. The results show how different methodological approaches may create complementary knowledge.

In 2008 our department was invited to participate in the creation of a permanent workshop promoting research about cancer in primary care; The Cancer and Primary Care Research International Network (Ca-PRI) [45]. This forum has proved to be an inspiration for many researchers in primary care, generating ideas and developing new ways and new standards for producing good knowledge about all aspects of cancer, with early diagnosis and cancer care as backbones. The important role of primary care in providing research-based knowledge about cancer, has been highlighted [46]. Now, in 2021, a first nationwide formal GP research practice network is about to be established in Norway.

To-day, it would be impossible to reproduce the delay findings based on the subjective criteria from the 1970s. A more modern approach emphasises the different intervals and milestones from first symptom to start of treatment, and encourages shortening of the different intervals with patients, GPs, hospital doctors and the administrative system as stakeholders. Not only the intervals from symptom to consultation, and from consultation to diagnosis counts: the time from diagnosis to first treatment is important as well [47]. The intervals have been clarified and standardised for research purposes [48, 49], and the Ca-PRI workshop is an active hot-spot for ideas and discussions.

In the last decade, many countries have organised different kinds of ‘fast track’ for patients suspected to have cancer [50]. This has helped shortening the time from symptom to treatment, which is in itself a good thing, and there is hope that it could also contribute to lowering cancer mortality.

One welcome result of Ca-PRI connections was a six-country study of a new cohort of general practice patients, focusing on abdominal symptoms. Consultation data were collected in 2011, and cancer was registered prospectively after six months or more. A question to the GPs about cancer suspicion now distinguished between different reasons for such suspicion: symptoms, clinical findings, intuition.

14.5 Results

Unexpectedly, in statistical analyses intuition ranged higher than symptoms or clinical findings in the association with a subsequent new cancer [51]. The study further demonstrated that a wide range of symptoms may signal abdominal cancer, with 'rectal bleeding' reaching the highest association with cancer. PPV above 3% was found for visible bleeding in the urine or from rectum, and for weight loss that was associated with a more specific abdominal symptom [52].

An analysis of the subgroup with colorectal cancer demonstrated clinically important differences between colon and rectal cancer, and between proximal and distal colon cancer. Proximal colon cancer often has scarcity or slow debut of symptoms, slow development of anaemia and fewer positive findings on clinical examination, which may explain more urgent but less fast track referrals and less implication of the GP in the initiation of diagnosis. The challenges of the GP's work is discussed in the article [53].

14.6 Short reflection

Again, GPs' clinical competence seems to be essential for the work with early diagnosis of cancer. A process of better understanding of diagnostic approaches towards symptom poor cancer is ongoing and will need further research.

The results from these studies seem to suggest why GPs working professionally quite often may arrive at correct cancer suspicions [42]. At the same time, the subjective assessment of probability will always be influenced by ideas about similarity or representativeness or other prior notions which easily may bias conclusions [54]. It would have been too much to expect that GPs could correctly suspect all subsequent cancers. One fourth of cancer cases in the six-country study were not suspected by the GP, but with good clinical training it should be possible to lower this proportion in the future.

In the UK, the NICE guidelines [55] give GPs a rational way to deal with probabilities. Patients suspected of cancer should be referred when the positive predictive value reaches 3%. This may be a surprisingly low risk threshold, but a single symptom by itself usually has a lower PPV [56]. The seemingly low PPV of 3.7% for any warning signal in relation to cancer that was reported in 1991 [26] might well justify a referral in some cases. Later studies referred to here, seem to support this.

15. Summing up/conclusion

15.1 Avoiding patient delay

What can the layman do to react rationally to signals from the body? First, it is important to know your own body. A few common symptoms should always have an explanation, especially if your age or habits put you in a risk group for a certain cancer. Bleeding unexpectedly from a body orifice is perhaps the most important of such symptoms. Often one can understand that some innocent condition caused

it, but if not, see your GP. The same way of thinking goes for a lump that is new or changing in size, for a mole growing or changing in colour, or a sore that does not heal. Cancer lodged deep in the body is more difficult, needing a certain size before signalled in the body. Cancer in an early stage is rarely painful. Pain may still be a relevant symptom, but you should know that pain is more than other symptoms caused by numerous non-cancerous conditions. Sometimes the best you can do is to observe and react to unexpected changes in the body, especially when they do not go away when you think they should.

15.2 Promoting early diagnosis in general practice

This article follows some of the stepstones leading up to present-day thinking about the early diagnosis of cancer. Some findings are in line with wise thoughts written even more than 40 years ago: Cox [57] worked in medical education and had been a professor of surgery before that. He wrote that “..beliefs about how likely different events and outcomes are derived from some facts, some habits and some hopes.” Cox listed five important factors which are quoted backwards, in order to start with the most basic: Fifth, decisions are based on subjective probabilities, not objective probabilities. Fourth, probabilities are about this individual 50 year-old male with both his cough and his unique genetic, family, socio-economic mix and disease history, not only any 50 year-old male with a cough. Third, what clinicians need is a probability given that symptom, not incidence figures. Second, clinicians think in probabilities in rather course categories, such as common, possible, rare. And first, when a probability is very low, its exact quantity is not important.

His further discussion is well worth reading, too. However, his article suffers the same lack of visibility as many early papers: the journal in question has been digitalised only from 2002. Again, try a university library.

Hence, how is this to be summed up for to-day's GPs?

1. Explain unusual symptoms

The vocational training of doctors should make them acquainted with the literature about warning signals, or alarm symptoms, as they are also called. Some symptoms like unexpected bleeding always need an explanation: Although often having a benign cause, it is important to exclude serious disease like cancer. Sometimes the distinction between symptoms and signs is blurred: In the early cancer context, anaemia is most often a sign discovered through the GP's blood tests rather than something the patient feels.

2. Add results from clinical findings and testing to symptoms

Most patients with cancer consult when their cancer can still be treated with a curative intent. This is motivating for a GP's work. In an early stage, less than half of cancer patients present with a warning signal in the consultation, but more than half have a warning signal and/or some other cancer relevant but low-risk symptom. Adding findings from clinical examination and testing, the GP will be able to suspect cancer in about four of five cases a short time after a patient consults [43].

3. Refer when the probability based on symptoms and findings exceed 3%

Usually, a GP needs some other information pointing in the same direction as the symptom, or replacing the symptom, to revise a PPV above the 3% NICE

level. If you do your GP job and examine carefully, you may even add your intuitive suspicion, which has been shown to be of importance.

4. Consider 'fast track' when you seriously suspect cancer

Patients with a warning signal have a greater probability to be referred to cancer patient pathways. The difficult challenge for GPs is to pursue more vague symptoms and refer relevant patients when a suspicion persists. Ordinary, comprehensive GP clinical work, attentive to details and to who the patient is, can facilitate this.

5. Last, but not least: Think of early diagnosis of cancer as an important, challenging, and interesting part of your effort to serve the patients who consult you!

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References

- [1] Berger J, Mohr J. A fortunate man. London: Canongate; 1967.
- [2] Bentsen B. The accuracy of recording patient problems in general practice. *J Medic Educ.* 1976;51:311-6.
- [3] Editorial: The image of cancer. *Lancet.* 1975;1(7919):1284.
- [4] Miller DG. What is early diagnosis doing? *Cancer.* 1976;37(S1):426-32. doi:10.1002/1097-0142(197601)37:1+<426::Aid-cncr2820370704>3.0.Co;2-p
- [5] Pack G, Gallo J. The culpability for delay in the treatment of cancer. *American Journal of Cancer.* 1938;33:443-62.
- [6] Leach J, Robbins G. Delay in the diagnosis of cancer. *JAMA.* 1947;135:5-8.
- [7] McWhinney I. The early diagnosis of cancer. Five years' experience in general practice. *J R Coll Gen Pract.* 1962;5:404-14.
- [8] Starey CJ. The diagnosis and treatment of cancer in a general practice. *J Coll Gen Pract.* 1966;12(1):32-42.
- [9] Feinstein AR, Pritchett JA, Schimpff CR. The epidemiology of cancer therapy. IV. The extraction of data from medical records. *Ann Intern Med.* 1969;123:571-90.
- [10] Holtedahl KA. [Diagnosis of cancer in general practice. I. Can diagnosis be made earlier?]. *Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke.* 1980;100(19-21):1219-23. English summary. . Available from: <https://hdl.handle.net/10037/12542>.
- [11] Holtedahl KA. [Diagnosis of cancer in general practice. II. What can the general practitioner improve? Case reports as a teaching aid]. *Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke.* 1980;100(19-21):1224-6. Available from: <https://hdl.handle.net/10037/12539>.
- [12] Gray DJP. The role of the general practitioner in the early detection of malignant disease. *Transactions Hunterian Soc (London).* 1966;25:121-75.
- [13] Cobb B, Clark RL, Jr., Mc GC, Howe CD. Patient-responsible delay of treatment in cancer; a social psychological study. *Cancer.* 1954;7(5):920-6. doi:10.1002/1097-0142(195409)7:5<920::aid-cncr2820070516>3.0.co;2-r
- [14] Hackett TP, Cassem NH, Raker JW. Patient delay in cancer. *The New England journal of medicine.* 1973;289(1):14-20. doi:10.1056/NEJM197307052890104
- [15] Howson JY. Observations on the delay period in the diagnosis of pelvic cancer. *Med Clin North Am.* 1948;32:1573-81. doi:10.1016/s0025-7125(16)35623-1
- [16] Jenkins S. Diagnostic delay in neoplastic disease. *J R Coll Gen Pract.* 1978;28(197):724-8.
- [17] Macadam DB. A study in general practice of the symptoms and delay patterns in the diagnosis of gastrointestinal cancer. *J R Coll Gen Pract.* 1979;29(209):723-9.
- [18] White KL, Williams TF, Greenberg BG. The ecology of medical care. *The New England journal of medicine.* 1961;265:885-92. doi:10.1056/NEJM196111022651805
- [19] Holtedahl KA. [Cancer diagnosis in general practice III-VII. The general

practitioner's recording of cancer warning signals in their patients. IV. Recording of interviews on cancer warning signals. Patients in general practice and in the general population. V. Patients with and without cancer. Who consults the physician for the 7 warning cancer signals? VI. The content of the warning signals. Is persistent pain relevant as a warning signal? VII. Alarm bell symptoms, alarm bell data and pitfalls. Some useful reminders for the general practitioner's work in cancer diagnosis]. English summary. Tidsskrift for den Norske laegeforening. 1984;104(12):799-812. Available from: <https://hdl.handle.net/10037/12543> ; <https://hdl.handle.net/10037/12544> ; <https://hdl.handle.net/10037/12545> ; <https://hdl.handle.net/10037/12547> ; <https://hdl.handle.net/10037/12548>.

[20] Høltedahl KA. The value of warning signals of cancer in general practice. *Scand J Prim Health Care*. 1987;5(3):140-3. doi:10.3109/02813438709013994

[21] Høltedahl KA. Inter-observer variation on registration of signals of cancer. *Scand J Prim Health Care*. 1987;5(3):133-9. doi:10.3109/02813438709013993

[22] Nylenna M. Diagnosing cancer in general practice: from suspicion to certainty. *Br Med J (Clin Res Ed)*. 1986;293(6542):314-7. doi:10.1136/bmj.293.6542.314

[23] Nylenna M, Gundersen S, Johannessen JV, (eds). *Kreft i almenpraksis [Cancer in General Practice]*. Oslo: Landsforeningen mot kreft, Universitetsforlaget; 1985. In Norwegian.

[24] Sackett DL, Haynes R, Tugwell P. *Clinical epidemiology. A basic science for clinical medicine*. . First edition. (Second edition 1991) ed. Boston: Little, Brown and Company; 1985.

[25] Bland M. *An introduction to medical statistics*. Oxford: Oxford University Press; 1987.

[26] Høltedahl KA. *Diagnosis of cancer in general practice. A study of delay problems and warning signals of cancer, with implications for public cancer information and for cancer diagnostic strategies in general practice (Thesis)* University of Tromsø, Norway: ISM skriftserie nr. 16, 1991. : <http://hdl.handle.net/10037/2325>

[27] Høltedahl KA. *Early diagnosis of cancer in general practice. A manual*. Berlin: Springer Verlag; 1990.

[28] Chapter 4. The use of diagnostic information to revise probabilities. In: Weinstein MC, Fineberg, H.V, editor. *Clinical decision analysis*. Philadelphia: W.B. Saunders Company; 1980.

[29] Høltedahl KA. A method of calculating diagnostic indexes for possible cancer symptoms in general practice. *Allgemeinmedizin*. 1990;19:74-9. Available from: <http://hdl.handle.net/10037/12484>.

[30] Høltedahl KA. More diagnostic indexes from general practice for some important forms of cancer. *Allgemeinmedizin*. 1990;19:80-5. Available from: <https://munin.uit.no/handle/10037/12487>.

[31] Høltedahl KA. Probability revision in general practice: the cases of occult blood in stool in patients with indigestion, and daily smoking in patients who cough. *Allgemeinmedizin*. 1990;19:35-8. Available from: <http://hdl.handle.net/10037/12453>.

[32] Mansson J, Bjorkelund C, Hultborn R. Symptom pattern and diagnostic work-up of malignancy at first symptom presentation as related to level of care. A retrospective study from the primary health care centre area of Kungsbacka, Sweden. *Neoplasma*. 1999;46(2):93-9.

- [33] Buntinx F, Wauters W. The diagnostic value of macroscopic haematuria in diagnosing urological cancers: a meta-analysis. *Family Practice*. 1997;14:63-8.
- [34] Holtedahl K. Research and practice combined--ideas for a life in general practice. *Fam Pract*. 2008;25(2):132-6. doi:10.1093/fampra/cm002
- [35] Bruyninckx R, Buntinx F, Aertgeerts B, Van Casteren V. The diagnostic value of macroscopic haematuria for the diagnosis of urological cancer in general practice. *Br J Gen Pract*. 2003;53(486):31-5.
- [36] Hamilton W, Round A, Sharp D, Peters TJ. Clinical features of colorectal cancer before diagnosis: a population-based case-control study. *Br J Cancer*. 2005;93(4):399-405. doi:10.1038/sj.bjc.6602714
- [37] Hamilton W. The CAPER studies: five case-control studies aimed at identifying and quantifying the risk of cancer in symptomatic primary care patients. *Br J Cancer*. 2009;101:S80-S6.
- [38] Jones R, Latinovic R, Charlton J, Gulliford MC. Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. *BMJ*. 2007;334:1040-4. doi:10.1136/bmi.39171.637106.AE
- [39] Lyratzopoulos G, Neal RD, Barbiere JM, Rubin GP, Abel GA. Variation in number of general practitioner consultations before hospital referral for cancer: findings from the 2010 National Cancer Patient Experience Survey in England. *Lancet Oncol*. 2012;13(4):353-65. doi:10.1016/S1470-2045(12)70041-4
- [40] Rubin G, Vedsted P, Emery J. Improving cancer outcomes: better access to diagnostics in primary care could be critical. *Br J Gen Pract*. 2011;61(586):317-8. doi:10.3399/bjgp11X572283
- [41] Ingebrigtsen SG, Scheel BI, Hart B, Thorsen T, Holtedahl K. Frequency of 'warning signs of cancer' in Norwegian general practice, with prospective recording of subsequent cancer. *Fam Pract*. 2013;30(2):153-60. doi:10.1093/fampra/cms065
- [42] Scheel BI, Ingebrigtsen SG, Thorsen T, Holtedahl K. Cancer suspicion in general practice: the role of symptoms and patient characteristics, and their association with subsequent cancer. *Br J Gen Pract*. 2013;63(614):e627-35. doi:10.3399/bjgp13X671614
- [43] Scheel BI, Holtedahl K. Symptoms, signs, and tests: The general practitioner's comprehensive approach towards a cancer diagnosis. *Scand J Prim Health Care*. 2015;33(3):170-7. doi:10.3109/02813432.2015.1067512
- [44] Johansen ML, Holtedahl KA, Rudebeck CE. How does the thought of cancer arise in a general practice consultation? Interviews with GPs. *Scand J Prim Health Care*. 2012;30(3):135-40. doi:10.3109/02813432.2012.688701
- [45] The Cancer and Primary Care Research International Network (Ca-PRI) [Internet]. [cited 13 June 2021]. Available from: <https://www.ed.ac.uk/usher/cancer-primary-care-research-international-network>.
- [46] Rubin G, Berendsen A, Crawford SM, Dommett R, Earle C, Emery J, et al. The expanding role of primary care in cancer control. *The Lancet Oncology*. 2015;16(12):1231-72. doi:http://dx.doi.org/10.1016/S1470-2045(15)00205-3
- [47] Hanna TP, King WD, Thibodeau S, Jalink M, Paulin GA, Harvey-Jones E, et al. Mortality due to cancer treatment delay: systematic review and meta-analysis. *BMJ*. 2020;371:m4087. doi:10.1136/bmj.m4087

- [48] Olesen F, Hansen RP, Vedsted P. Delay in diagnosis: the experience in Denmark. *Br J Cancer*. 2009;101 Suppl 2:S5-8. doi:10.1038/sj.bjc.6605383
- [49] Weller D, Vedsted P, Rubin G, Walter FM, Emery J, Scott S, et al. The Aarhus statement: improving design and reporting of studies on early cancer diagnosis. *Br J Cancer*. 2012;106(7):1262-7. doi:10.1038/bjc.2012.68
- [50] Holtedahl K. Challenges in early diagnosis of cancer: the fast track. (Editorial). *Scand J Prim Health Care*. 2020;38(3):251-2. doi:10.1080/02813432.2020.1794415
- [51] Holtedahl K, Vedsted P, Borgquist L, Donker GA, Buntinx F, Weller D, et al. Abdominal symptoms in general practice: Frequency, cancer suspicions raised, and actions taken by GPs in six European countries. Cohort study with prospective registration of cancer. *Heliyon*. 2017;3(6):e00328. doi:10.1016/j.heliyon.2017.e00328
- [52] Holtedahl K, Hjertholm P, Borgquist L, Donker GA, Buntinx F, Weller D, et al. Abdominal symptoms and cancer in the abdomen: prospective cohort study in European primary care. *Br J Gen Pract*. 2018;68(670):e301-e10. doi:10.3399/bjgp18X695777
- [53] Holtedahl K, Borgquist L, Donker GA, Buntinx F, Weller D, Campbell C, et al. Symptoms and signs of colorectal cancer, with differences between proximal and distal colon cancer. A prospective cohort study of diagnostic accuracy in primary care. *BMC Family Practice*. 2021. DOI: 10.1186/s12875-021-01452-6
- [54] Tversky A, Kahneman D. Judgment under Uncertainty: Heuristics and Biases. *Science*. 1974;185(4157):1124-31. doi:10.1126/science.185.4157.1124
- [55] Suspected Cancer: Recognition and Referral (NICE guideline 12). London
2015. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/26180880>.
- [56] Shapley M, Mansell G, Jordan JL, Jordan KP. Positive predictive values of $\geq 5\%$ in primary care for cancer: systematic review. *Br J Gen Pract*. 2010;60(578):e366-77. doi:10.3399/bjgp10X515412
- [57] Cox KR. The GP and the cancer patient. What does a GP do about the person who might have cancer? *Australian Family Physician*. 1978;7(June):757-68.