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COMPUTER-ASSISTED FOLLOW-UP FOR THYROID DISEASE



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The Need for Continuing Care

There is increasing recognition in many specialties of the difficulties faced by clinicians in maintaining long-term contact with patients, both for individual care and for evaluation of their management. A review of specialty and general medical journals in the United States and Great Britain reveals an increasing number of reports on this subject. For example, the clinical indications of these follow-up studies have included gastrointestinal surgery, celiac disease, cardiovascular disease, drug abuse, glaucoma, endocrinology and diabetes, and schizophrenia and other psychiatric disorders. In many of these reports, clinicians describe the use of specially designed follow-up registers to ensure continuity of care. The main problems are: first, losses to follow-up with the subsequent development of complications, and second, failure to collect information for evaluation purposes on the outcome of treatment from both well and sick patients. Interruption of follow-up is often unintentional on the part of physicians and their patients. But with the increasing mobility of people, it is inevitable in a substantial proportion of the treated population at some point in their lifetime.

It might be argued that it makes economic sense, and is ethically obligatory, to provide a physician- or health-service-initiated follow-up system to ensure that the initial beneficial effects of a treatment are maintained by detecting new events that occur either because of the natural history of the disease or as iatrogenic complications. The ethical arguments are particularly strong when treatment is essentially empirical and includes procedures such as the therapeutic use of isotopes.

In the report that follows, I will attempt to describe the level of need for continuing medical care for patients with thyroid disease and argue the case for an approach in which responsi-

bilities for such care are shared by specialists, primary care physicians, and patients. Finally, the report provides clinical data from several long-term follow-up studies based on a computer-assisted thyroid follow-up register.

The Case for Thyroid Follow-up

Radioiodine treatment. The need for surveillance here is well established. In a review of 2,493 patients, treated by radioiodine for hyperthyroidism during the previous 15 years in four Scottish centers, 1,257 (50%) were receiving thyroxine (Scottish Automated Follow-up Register Group, unpublished statistics, 1981). In patients who were euthyroid at that time, the subsequent ten-year cumulative incidence of hypothyroidism ranged from 22% (95% confidence limits [CL], 9% to 35%) in patients receiving 1 to 5 mCi, and up to 45% (95% CL, 28% to 62%) in those treated with 16 to 20 mCi (Table 1). It is now clear that hypothyroidism is unavoidable in many patients in spite of the use of precision dosimetry, low-dose techniques, and different isotopes.^{1,3}

Table 1

Total dose ¹³¹ I (mCi)	Ten-year incidence hypothyroidism (%)	95% Confidence limits
1-5	22	9-35
6-10	31	24-37
11-15	30	13-46
16-20	45	28-62

Table 1

Cumulative incidence rates of hypothyroidism after radioiodine therapy for hyperthyroidism (life-table analysis) from the Scottish Automated Follow-up Register (SAFUR) follow-up program in four centers.

Subtotal thyroidectomy. In the United States and Great Britain, surgery for Graves' disease is followed by hypothyroidism in 20% to 40% of patients.^{4,6} In patients with larger thyroid remnants and persisting thyroid-stimulating immunoglobulins, recurrences will continue to appear for more than 20 years postsurgery.⁷

Thyroxine replacement. Studies in the United States and Great Britain have shown that patients with chronic disease

often do not take long-term medication in the recommended dosage and, sometimes, stop taking medication altogether, either on their own initiative or because of advice from another physician.^{8,9} This problem frequently arises in thyroid patients; in one of the original reviews by our group, 75% of those taking thyroxine were undertreated.⁵

The risk of future complications occurring over a long period of time is now largely predictable. It seems reasonable to propose that the provision of health care should be designed to meet this need. Most thyroid specialists would prefer to retain contact and clinical control over all the patients they treat. However, in the British health service, the numbers of patients seen for routine follow-up at specialist outpatient clinics increasingly restrict the use of these facilities for patients with difficult problems and new referrals. In many centers, therefore, alternative approaches are being sought that will provide a minimum standard of care for *all* patients, and more care for those in special need.

Design and Use of Registers

The objectives of long-term follow-up in thyroid disease and the principle of sharing the organization of medical work between specialty clinics and primary care were first advanced by Crooks.¹⁰ The application of these ideas in a manual follow-up system followed and, later, computer-based versions were developed in Aberdeen and Birmingham.¹¹⁻¹³ Over the next 15 years, similar systems have been adopted in 11 centers throughout Great Britain.

The present Scottish Automated Follow-up Register (SAFUR) serves thyroid clinics, 1,550 general practitioners, and about 9,500 patients in five Scottish cities and their health districts. New patients now are being registered at the rate of 500 per year, and plans are being made to increase this figure. The thyroid physician using SAFUR can register a patient either at the time of first treatment, such as radioiodine therapy or subtotal thyroidectomy, or when the patient is euthyroid, stabilized, and ready for discharge from the clinic. At this point, follow-up is activated and the register takes over coordination of all further reviews. The register functions as a sun-satellite system with a large central registry carrying out, for each participating center, the scheduling of examinations at stipulated intervals, correspondence with physicians and patients, and analysis of thyroid function tests (TFTs). The initial test used in screening is confined to a T₄ concentration by radioimmunoassay. For recalled patients, additional tests, including serum thyrotropin determination, were used to establish the diagnosis. (The new screening procedure includes the use of both serum T₄ and thyroid-stimulating hormone as screening tests.) Results are reported to both the hospital clinic and the general practitioner. The system is linked to the National Health Service Central Register, which receives automatic notification of deaths with an abstract of the death certificate (Figure 1).

If the general practitioner is unable to use the system, the patient is still offered registration and follow-up. The register then uses the nearest clinic or laboratory as the screening agent of first contact.

The system uses a two-tier screening procedure. In the first instance, the results of TFTs are automatically partitioned into two groups, those within the local reference range and those above or below it. No further action is taken on the normal results, but listings of patients with abnormal tests are examined by a thyroid physician, with supplementary records if necessary. The clinical decisions made at this point usually lead to many of the "abnormal" patients being graded as normal and their follow-up continues uninterrupted. The remainder are either reassessed by their general practitioner or, as is usual,

they are seen at a thyroid clinic and, if necessary, offered treatment to restabilize their thyroid state.

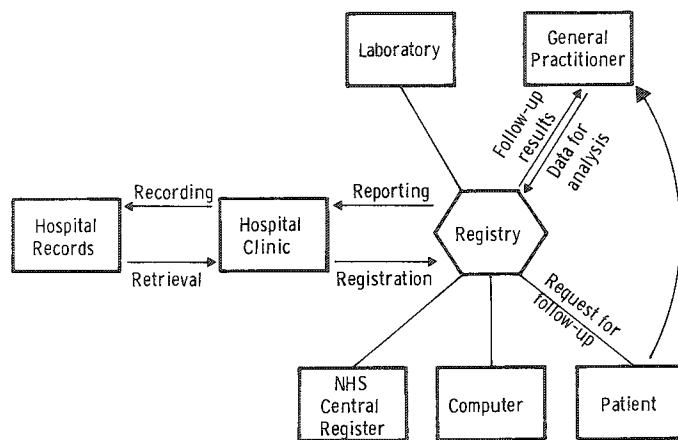


Figure 1
Scottish Automated Follow-up Register showing links with thyroid clinic, general practitioner, patient, and National Health Service Central Register.

Studies Based on SAFUR

The system offers good opportunities for clinical and epidemiological research. It provides cumulative personal records for a defined population with complete follow-up. The use of actuarial analyses of the follow-up data yields incidence rates adjusted for person-years of exposure and events other than the particular outcome that is being measured. A selection of routine data and special studies illustrates the potential of this type of clinical information system.

Postsurgical hypothyroidism. Nofal et al found that patients treated for Graves' disease by subtotal thyroidectomy and followed up in the Mayo Clinic showed an annual incidence of late-onset hypothyroidism of 1.7%.⁴ Other reports have disputed this finding, and studies in Great Britain using conventional medical records failed to confirm it.^{6,14,15} SAFUR recently used the files of a total of 839 patients under continuous surveillance to show that in one center the predicted ten-year incidence of late-onset hypothyroidism was 7.4% (95% CL, 3.8% to 11.1%), and in another center 10.8% (95% CL, 3% to 18.6%).¹⁶ All of these patients had been euthyroid and stable for 12 months after surgery and before entry to the follow-up system. Many centers do not follow up patients who achieve a euthyroid state one year after operation, but in the light of these results their policy should be reviewed.

Thyroxine replacement. In a recent study, the records of 2,710 thyroxine-treated patients were analyzed to determine the frequency of recognized under- or overtreatment with thyroxine.¹⁷ The overall ten-year incidence of undertreatment was 13% (95% CL, 11% to 16%). These data can be broken down into rates for noncompliance and apparent increased metabolic requirements (Figure 2). In four centers using SAFUR, the median six-year incidence of overtreatment was 6.2%. Thus, even under near optimal conditions for follow-up, an appreciable risk of problems with replacement therapy is developing. In this series they all were corrected, on average, within seven months of onset; but without a prescribed follow-up plan many are likely to have been undetected for longer periods. The register now provides a model in which to evaluate the effect of improved patient (and physician) education about the management of replacement therapy.

Antithyroid drugs. In Glasgow, Young et al recently have used the computer-held files of a thyroid register to link records in several different hospitals and identify all patients originally

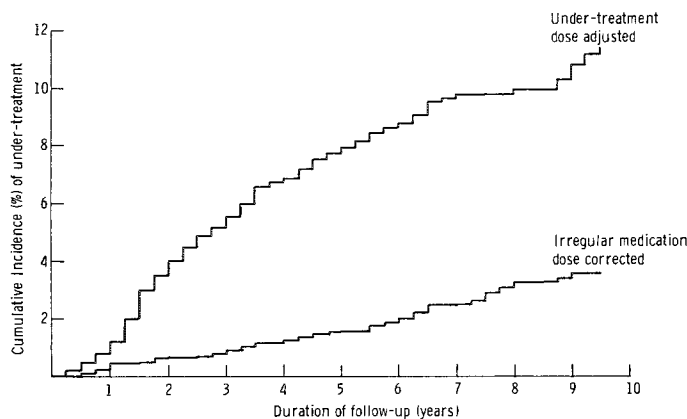


Figure 2
Cumulative incidence (life-table analysis) of undertreatment in 2,710 patients treated with thyroxine replacement therapy.

given antithyroid drugs (ATD) as definitive treatment.¹⁸ The outcome of follow-up in 434 unselected patients over 2 to 25 years (mean, ten years) has provided new information that may be useful for planning management with ATD. For example, the overall five-year recurrence rate (95% CL) was 55% to 61%. However, those patients whose thyroid uptake was suppressed with triiodothyronine, on completion of their course of drugs, showed recurrence rates of only 25% to 40%, compared with 85% to 89% for those not suppressed. The proportion of suppressed patients was higher in those treated longer than six months. Furthermore, within the suppressed group, a higher proportion achieved a lasting remission among those treated longer than six months compared with shorter courses. In suppressed patients, the overall accuracy of the test in predicting lasting remission was 77%, which compares favorably to other approaches.¹⁹

Breast cancer and thyroid disease. There has been a long-standing debate about causal links between thyroid disease, its treatment, and the risk of breast cancer. Some studies in recent years have received unbalanced publicity in the media. This caused serious concern among some thyroid patients, especially those taking thyroxine. SAFUR was used to examine the incidence of breast cancer in 2,523 patients, who were registered and followed up in one geographical area.²⁰ The study showed that the overall ten-year cumulative incidence of breast cancer in thyroid patients ($1.54\% \pm 0.42$ SE) was similar to the expected rate (1.5%) for a population of the same age and sex. There was no excess risk of breast cancer in any subgroup defined by age, previous radioiodine or surgical treatment, autoimmune thyroiditis, or thyroxine replacement (Table 2). SAFUR will continue to review this issue at intervals as the population exposure increases.

Diagnostic accuracy and loss to follow-up. SAFUR monitors its own performance. One aspect of this is the efficiency of the screening procedure. Table 3 shows the false-positive rates and predictive power of a positive screening test result (serum thyroxine) in 4,787 follow-up examinations. Initially, 290 (6%) tests fell outside the reference range. Scrutiny of patient records by a physician led to 132 (46%) of these being passed and followed up reactivated.

The remaining 158 patients were reassessed at a thyroid clinic; 97 (61%) were considered to need further treatment. Seven patients with a negative screening test were sent back before their next follow-up examination, and six were found to have significant abnormalities. In the two-tier screening system, the predictive power of the screening procedure is acceptable but needs improvement. Further refinements can and will be introduced, such as serum thyrotropin levels in selected patients.

Table 2

Population	Total in group	Breast cancer		Relative risk* (± 1 SE)
		Total observed	Total expected	
All	2,523	22	20.83	0.85–1.31
Hyperthyroidism				
Radioiodine-treated	714	7	6.7	0.71–1.54
Surgically treated	1,006	9	8.38	0.76–1.52
Autoimmune thyroiditis				
Thyroxine-treated	429	2	2.97	0.38–1.20
Thyroxine-treated†				
All patients	1,847	19	16.38	0.91–1.48
Non-thyroxine-treated				
All patients	953	7	7.24	0.67–1.4

*Relative risk = observed cases of breast cancer/expected cases of breast cancer.

†Includes some patients from the non-thyroxine-treated group who became hypothyroid during follow-up.

Table 2

Incidence of breast cancer in a thyroid population: The relative risk shows no significant departure from unity.

Table 3

Screening test result based on serum thyroxine level

Final result of independent assessment	No recall	Recall	Total
	No recall	4,490	132
Unnecessary recall	1	61	62
Significant abnormality	6	97	103
Total	4,497	290	4,787

Table 3

SAFUR: Two-tier system of screening for abnormal thyroid status. In 4,787 examinations, the initial phase, using serum thyroxine results, yields 290 (6%) abnormal tests. Assessment by a physician leads to 158 patients being recalled, of whom 97 (61%) received further treatment. Seven patients with a negative screen were later sent back by their general practitioner; six patients were found to have significant abnormalities.

However, we have been cautious about introducing additional tests without evidence that the increased cost will be matched by significant improvements in the efficiency of screening.

Another aspect of internal audit is the review of patients who are lost to follow-up.²¹ When patients move without notice, the registry makes concerted efforts to trace them when a follow-up examination is due. Cumulative incidence curves can be used to examine the performance of each center in preventing losses and determining the reasons for discontinued follow-up (Figure 3). Through the thyroid register's link with the National Health Service Central Register, it is possible to trace patients who have moved, providing they join a general practitioner's list in their new area. Contact with the patient is reestablished only with the permission of their new physician. Patients and their physicians may withdraw from the system but few take this option.

Cost-effectiveness

The concept of a thyroid follow-up system arose in the 1960s. It

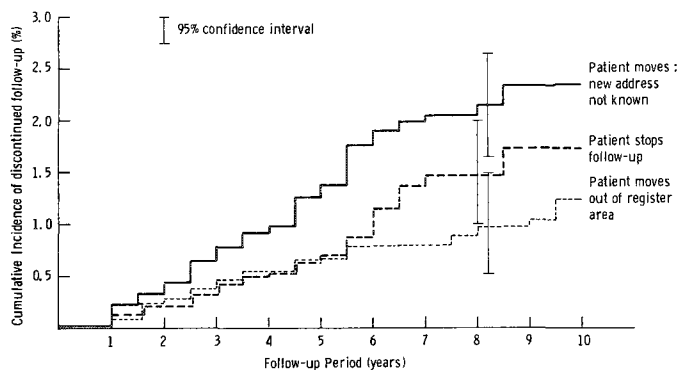


Figure 3
Cumulative incidence (life-table analysis) of losses to follow-up for different reasons in four centers.

might be argued that in light of current widespread knowledge about the need for long-term surveillance, we now could dispense with registers. This study was recently undertaken to determine the most efficient use of resources by comparing the level of surveillance (medical work done), long-term outcome (prevalence of undetected hypothyroidism), and costs of follow-up by conventional health care (952 patients), and a follow-up register (702 patients).²² All patients had been treated by radioiodine for hyperthyroidism over the same ten-year period. Attempts were made to trace and assess the thyroid status of the conventional care group; the computer-held records of the register group were analyzed using the same criteria. Only 712 (74%) of the conventional care group could be traced and recalled over the period of a year. Losses in the sample of register patients amounted to 1.4% (Table 4).

Table 4

	Conventional care	Register follow-up
Lost to follow-up (%)	26	1.4
Follow-up contacts per year	1.54	0.82
Prevalence of hypothyroidism at last follow-up (%)	19	7
Annual follow-up costs (dollars)	21	9.8

Table 4
Cost-effectiveness of register-based follow-up compared with conventional care: Losses to follow-up, medical work, undetected hypothyroidism, and average annual follow-up costs.

The study showed that, on average, nearly twice as much medical work was done for the conventional care group, but this only related to a minority of patients and, for many, follow-up had lapsed. The prevalence of undetected hypothyroidism was 19% in the conventional care patients, compared to 7% of the register population who were found to have an abnormal screening test at their last follow-up. The costs of follow-up for

the register patients, if costs of treating hypothyroidism are included, were less than 60% of that for those receiving conventional care.

It seems clear that without some form of prescribed follow-up plan, long-term care may be highly variable, and that, at least within the context of the British health service, the register approach is the most cost-effective method of managing the follow-up of a thyroid population.

The Future of Registers

In the long-term management of thyroid disease, there is a need to build into our clinical information collection procedures the type of measures that are needed for evaluation. The follow-up system described here is only the minimum facility required, and many refinements now could be added. Furthermore, it now is possible to conceive of alternatives and modifications that place greater emphasis and responsibility on the patient, and on the general practitioner or specialist; however, it would be necessary to show that they were equally cost-effective.

The present register runs on a mainframe computer with batch-processing. It will soon be necessary to develop new program suites for microprocessors. In SAFUR, such interactive systems will allow greater decentralization of follow-up for routine patient care activities, but retain the facility for clinical and epidemiological research through periodic updating of files in the central registry. Such an approach is being developed by our group for diabetes.²³

Registers can improve general standards of care by ensuring that fail-safe procedures for follow-up are offered to everyone. On the other hand, large-scale unproductive testing of low-risk patients is, of course, unnecessary.

Good follow-up systems should provide clinical and statistical information that is needed to avoid such unnecessary screening. Clinical research now should concentrate on the development of screening procedures with high predictive power, thereby reducing costs to the system and inconvenience to the patient.

Finally, recent studies of high quality are again raising questions about excess morbidity and mortality risks in aging populations of thyroid patients.²⁴ This serves to reinforce my assertion that the onus is firmly on thyroid specialists to provide some form of fail-safe, long-term care to patients who may be at risk of new health problems arising many years after the original treatment.

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