Efficiency of hepatitis C virus screening strategies in general practice

Valérie JOSSET (1, 2), Jean-Philippe TORRE (1), Marie-Pierre TAVOLACCI (1), Vanessa VAN ROSSEM-MAGNANI (1), Karine ANSELM (1), Véronique MERLE (1, 2, 3), Jean GODART (4), Alain LIBERT (4), Joël LADNER (1, 2), Pierre CZERNICHOW (1, 2, 3)

(1) Département d’Épidémiologie et de Santé Publique, Centre Hospitalier Universitaire, Hôpitaux de Rouen ; (2) Réseau de Recherche sur le Système de Soins, (3) Réseau Hépatite C, Haute-Normandie ; (4) Médecin généraliste.

SUMMARY

Hepatitis C viral infection (HCV) is a frequent and severe disease; screening strategies to-date remain insufficient.

Objective — To assess the efficiency of HCV screening of high-risk groups among patients consulting general practitioners.

Methods — A cost-effectiveness analysis was performed involving general medicine screening practices recorded during a survey of 127 practitioners (10 041 patients) conducted in 1997. A reference strategy, defined as HCV screening for illicit drug users and transfused patients, and five extended strategies, where the screening population was broadened to include other risk groups as well, were considered. Average cost and marginal cost-effectiveness ratios were determined for each extended strategy and compared with those observed for the reference strategy. The sensitivity of HCV screening to funding modalities, HCV seroprevalence and proportion of HCV high-risk groups among patients attending general practitioners was studied.

Results — The reference strategy was the most cost-effective method irrespective of the funding modality considered. Fixed practitioner payment was the least efficient funding modality. The average cost of one positive test was sensitive to variations of HCV seroprevalence in the high-risk group as well as the proportion of high-risk patients among the general practitioners’ patients.

Conclusion — Extension of hepatitis C screening to risk groups other than transfused patients and illicit drug users implies a substantial increase in healthcare costs as well as social consensus for such expenditures.

The full text of this article is available in English, free of charge, on the web on: www.e2med.com/gcb.
ALAT was not retained for the present study which targeted asymptomatic persons.

Two large groups were thus defined for screening: subjects transfused before 1991 and illicit drug users (current or former intravenous injection or inhalation) [4-7]. Depending on the guidelines considered, other target groups are often proposed for screening: family of contaminated patients, sexual partners of HCV-positive subjects, healthcare personnel, prisoners or former prisoners [4-7]. Furthermore, for certain large population groups, e.g. subjects with a history of gastrointestinal endoscopy or invasive medical or surgical procedures, screening propositions may be contradictory due to uncertainty concerning mode of transmission [16-19]. The effectiveness of these different screening strategies has not been studied extensively [20-23].

Thus, despite the need for improved knowledge of risk factors, as well as the probable need for prior training to achieve optimal screening in the general medicine setting [24], the study was performed by general practitioners who play a key role as primary care givers for the majority of the risk groups in the general population.

The purpose of the present work was to compare the cost-effectiveness of different HCV screening practices performed in the general medicine setting during the pilot study.

Patients and methods

Patients

A pilot study on HCV screening was conducted in 1997 in Haute-Normandie, France. Voluntary physicians (n = 127) used a questionnaire to search for risk factors in all patients aged 18 to 70 years consulting during two five-day periods. A free HCV screening test was to be proposed to each patient who had at least one risk factor and whose HCV serology was not known. Screening tests were performed with 3rd generation ELISA which was considered to offer satisfactory sensitivity and specificity [4, 25]. Tests performed within ten days of consultation were retained for analysis.

Screening strategies

A reference screening strategy (S₀) was defined in compliance with official recommendations [4-7]: blood transfusion before 1991 or at unknown date, present or past use of illicit drugs by intravenous injection or inhalation. Five other screening strategies were defined from the data collected during the survey, each consisting of extending screening to a new risk group:

— history of gastroscopy (strategy S₁);
— contact with an infected person: spouse or other family member with hepatitis C, occupational exposure (physicians, nurses, ...), active or former imprisoned (strategy S₂);
— history of invasive procedures: catheterism, fluid aspiration/cytology, biopsy (strategy S₃);
— history of colonoscopy (strategy S₄);
— history of surgery (strategy S₅).

For each of these six strategies, the number of patients concerned in the physician’s practice and the number of positive serologies observed among patients with a formerly unknown HCV status were noted.

Cost estimates

Direct medical costs were considered exclusively: physician’s fees, test costs. Values were taken from the applicable reimbursement schedules (NGAP, Nomenclature Générale des Actes Professionnels) established by the French national health insurance fund as follows:

— blood sample 3.77 € — 100% reimbursement;
— ELISA 18.78 € — 100% reimbursement;

Three funding modalities were hypothesized to estimate the cost of general medicine screening practices:

— considering that a screening campaign does not change routine practices, that patients attend consultations for other medical problems and no extra costs ensue, screening is an integral part of routine medical care (modality T);
— considering that general practitioners receive fixed payment for screening, irrespective of the number of tests prescribed (modality F), two levels can be considered: Fa = 152.45 € and Fb = 228.67 €;
— considering that a public campaign increases the number of consultations (specifically for screening), practitioner activity is affected (modality C); three levels of increased activity can be considered: 10% (C₁₀%), 30% (C₃₀%), 50% (C₅₀%).

Hypothesizing a short screening campaign, all costs were fixed.

Cost-effectiveness analysis

Mean cost per case of HCV infection detected was calculated by dividing total cost by the number of positive serology tests. The marginal cost-effectiveness ratio [26] between strategy S₀ and each of the other strategies was determined by dividing the marginal cost by the number of additional positive serology tests. The sensitivity of considered marginal cost-efficiency ratios to variations in regional prevalence of HCV infection [27], differences in the prevalence of positive tests in each risk group, and the relative proportion of each risk group in the physician’s practice was also studied.

Results

Among the 10,041 patients included (mean age 44.3 ± 15.1 years, 62% female), 5,445 (54%) presented at least one of the risk factors studied. Among the 924 high-risk patients (804 patients who had a blood transfusion before 1991 or at an unknown date, 117 patients who used or had used illicit drugs by intravenous injection or inhalation, 3 patients with both risk factors), HCV status was known for 143 (15.5%), including 45 seropositive patients. Screening tests (n = 3550) performed for patients with at least one of the risk factors studied detected 49 positive patients (1.4%; 95%CI: 1.0-1.8). The prevalence of HCV infection was thus (45 + 49)/3550 = 2.6% (95%CI: 2.3-.2.9). Seroprevalence was not related to gender or age.

Cost-effectiveness of each strategy (table I)

Overall cost was lowest for strategy S₀, irrespective of the funding modality retained. This strategy accounted for 15.5% of the screening tests (551/3550) and detected 19 of the 49 positive serologies discovered (39%).

Two of the extended strategies produced a significant increase in the number of positive tests:

— strategy S₁ (extension to patients with a history of surgery, 43% of consulting patients) led to the detection of 15 more positive patients, i.e. 69% of the potentially positive tests, at the cost of a very large number of screening tests (74% of the 3550 potential tests).
— Strategy S₅ (extension to patients with a history of gastroscopy, 21% of consulting patients) led to detection of 8 more positive patients, i.e. 55% of the potentially positive tests, at the cost of only 1348 supplementary tests (38% of the 3550 potential tests).

The three other extended strategies (history of invasive procedures, contact with an infected person, colonoscopy) yielded at best five more positive tests than S₀. The mean cost of a positive test (table I) varied four fold from 654 € (S₀, cost of test...
Discussion

The data analyzed here were collected by general practitioners who participated in a screening practice study. These voluntary physicians may not have been representative of the general practitioner population for reasons related to their patient recruitment (proportion of illicit drug users among patients), their earlier screening practices, or their capacity to convince patients to have a screening test. Several results only to 2,589 € (S5, fixed payment modality Fa, 152.5 €). Globally, strategy S3 (extension to include contact with an infected person) yielded the lowest cost after S0, while strategy S2 (extension to history of surgery) was by far the most expensive. With fixed payment (modalities Fa and Fb) cost varied 1 to 1.4-fold, while for other funding modalities (T, C10%, and C50%), the range of cost was wider (1 to 2.6-fold).

Irrespective of the extension strategy or funding modality, the marginal cost-effectiveness ratio was higher than the mean cost of the reference strategy S0 (table III), particularly when the funding hypothesis differed from the level observed in the study, the marginal cost-effectiveness ratio rose rapidly for strategies S1 to S4 and progressively for strategy S5.

Sensitivity analysis

In the risk groups considered, there was an inverse relationship between seroprevalence and marginal cost-effectiveness ratio. As illustrated in figure 1 for strategy S1, a small decline in seroprevalence from 2% to 1.8% was associated with a strong 1.5-fold increase in the marginal cost-effectiveness ratio, irrespective of the type of funding. A similar pattern was observed for the other risk groups.

An inverse relationship was also observed between the marginal cost-effectiveness ratio and the proportion of the physician’s practice corresponding to the risk group (figure 2). When the proportion of patients in the designated group was hypothesized to declined from the level observed in the study, the marginal cost-effectiveness ratio rose rapidly for strategies S1 to S4 and progressively for strategy S5.

Table I. – Effectiveness and costs of HCV infection screening strategies according to different funding methods. Haute-Normandie, 1997.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Patients screened (n)</th>
<th>% of consulting patients</th>
<th>Tests performed</th>
<th>Tests performed (%)</th>
<th>Positive tests</th>
<th>Positive tests (%)</th>
<th>Cost hypotheses in 1000 €</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>T</td>
</tr>
<tr>
<td>S0</td>
<td>924</td>
<td>9.2%</td>
<td>551</td>
<td>15.5%</td>
<td>19</td>
<td>38.8%</td>
<td>12.4</td>
</tr>
<tr>
<td>S1</td>
<td>2148</td>
<td>21.4%</td>
<td>1348</td>
<td>38%</td>
<td>27</td>
<td>55.1%</td>
<td>30.4</td>
</tr>
<tr>
<td>S2</td>
<td>1209</td>
<td>12.0%</td>
<td>728</td>
<td>20.5%</td>
<td>20</td>
<td>40.8%</td>
<td>16.4</td>
</tr>
<tr>
<td>S3</td>
<td>1917</td>
<td>19.1%</td>
<td>1193</td>
<td>33.6%</td>
<td>23</td>
<td>46.9%</td>
<td>26.9</td>
</tr>
<tr>
<td>S4</td>
<td>1765</td>
<td>17.6%</td>
<td>1121</td>
<td>31.6%</td>
<td>24</td>
<td>49%</td>
<td>25.3</td>
</tr>
<tr>
<td>S5</td>
<td>4280</td>
<td>42.6%</td>
<td>2615</td>
<td>73.7%</td>
<td>34</td>
<td>69.4%</td>
<td>59.0</td>
</tr>
<tr>
<td>Total</td>
<td>10041</td>
<td></td>
<td>3550</td>
<td></td>
<td>49</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

S0: screening patients transfused before 1991 or at an unknown date and/or patients with a history of drug abuse; S1: S0 + screening for patients with a history of gastroscopy S2: S0 + screening for patients exposed to an HCV-infected person; S3: S0 + screening for patients with a history of invasive procedures (catheterism, fluid aspiration/cytology, biopsy); S4: S0 + screening for patients with a history of colonoscopy; S5: S0 + screening for patients with a history of surgery.

T: reimbursement of blood sample and test; C10%: T + 10% extra consultations; C30%: T + 30% extra consultations; C50%: T + 50% extra consultations; Fa: T + fixed payment (152.5 €); Fb: T + fixed payment (228.7 €).

Table II. – Average cost of one HCV positive test (in Euros) of different HCV infection screening strategies according to different funding methods. Haute-Normandie, 1997.

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Tests performed</th>
<th>Positive tests</th>
<th>Cost hypotheses (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>T</td>
</tr>
<tr>
<td>S0</td>
<td></td>
<td>924</td>
<td>551</td>
</tr>
<tr>
<td>S1</td>
<td></td>
<td>2148</td>
<td>1348</td>
</tr>
<tr>
<td>S2</td>
<td></td>
<td>1209</td>
<td>728</td>
</tr>
<tr>
<td>S3</td>
<td></td>
<td>1917</td>
<td>1193</td>
</tr>
<tr>
<td>S4</td>
<td></td>
<td>1765</td>
<td>1121</td>
</tr>
<tr>
<td>S5</td>
<td></td>
<td>4280</td>
<td>2615</td>
</tr>
</tbody>
</table>

S0: screening patients transfused before 1991 or at an unknown date and patients with a history of drug abuse; S1: S0 + screening for patients with a history of gastroscopy S2: S0 + screening for patients exposed to an HCV-infected person; S3: S0 + screening for patients with a history of invasive procedures (catheterism, fluid aspiration/cytology, biopsy); S4: S0 + screening for patients with a history of colonoscopy; S5: S0 + screening for patients with a history of surgery.

T: reimbursement of blood sample and test; C10%: T + 10% extra consultations; C30%: T + 30% extra consultations; C50%: T + 50% extra consultations; Fa: T + fixed payment (152.5 €); Fb: T + fixed payment (228.7 €).
Table III. − Marginal cost (in euros per HCV positive test) in HCV infection screening strategy extensions according to different funding methods. Haute Normandie, 1997.

<table>
<thead>
<tr>
<th>S0 à S1</th>
<th>T</th>
<th>C10%</th>
<th>C30%</th>
<th>C50%</th>
<th>Fa</th>
<th>Fb</th>
</tr>
</thead>
<tbody>
<tr>
<td>2247 €</td>
<td>2461 €</td>
<td>2889 €</td>
<td>3318 €</td>
<td>2247 €</td>
<td>2247 €</td>
<td></td>
</tr>
<tr>
<td>3991 €</td>
<td>4390 €</td>
<td>5188 €</td>
<td>5986 €</td>
<td>3991 €</td>
<td>3991 €</td>
<td></td>
</tr>
<tr>
<td>3619 €</td>
<td>3967 €</td>
<td>4662 €</td>
<td>5357 €</td>
<td>3619 €</td>
<td>3619 €</td>
<td></td>
</tr>
<tr>
<td>2571 €</td>
<td>2806 €</td>
<td>3277 €</td>
<td>3748 €</td>
<td>2571 €</td>
<td>2571 €</td>
<td></td>
</tr>
<tr>
<td>3103 €</td>
<td>3416 €</td>
<td>4043 €</td>
<td>4669 €</td>
<td>3103 €</td>
<td>3103 €</td>
<td></td>
</tr>
</tbody>
</table>

S0: screening patients transfused before 1991 or at an unknown date and/or patients with a history of drug abuse; S1: S0 + screening for patients with a history of gastroscopy; S2: S0 + screening for patients exposed to an HCV-infected person; S3: S0 + screening for patients with a history of invasive procedures (catheterism, fluid aspiration/cytology, biopsy); S4: S0 + screening for patients with a history of surgery.

F0: reimbursement of blood sample and test; C10%: T + 10% extra consultations; C30%: T + 30% extra consultations; C50%: T + 50% extra consultations; F0: T + fixed payment (152.5 €); F0a: T + lump sum fee (152.5 €); F0b: T + lump sum fee (228.7 €).

Fig. 1 − Impact of HCV seroprevalence on marginal cost-effectiveness ratios (euros per one positive HCV test) of one HCV positive test in HCV screening extended beyond the reference group (S0) to patients with a history of gastroscopy (S1). Haute Normandie, 1997.

Fig. 2 − Impact of the relative proportion of high risk groups among general practitioners’ patients on marginal cost-effectiveness ratios (euros per one positive HCV test) in each extended HCV screening strategy, considering the hypothesis of 30% extra general practitioner consultations. Haute Normandie, 1997.

S0: screening patients transfused before 1991 or at an unknown date and/or patients with a history of drug abuse; S1: S0 + screening for patients with a history of gastroscopy; S2: S0 + screening for patients exposed to an HCV-infected person; S3: S0 + screening for patients with a history of invasive procedures (catheterism, fluid aspiration/cytology, biopsy); S4: S0 + screening for patients with a history of surgery.

The values on the curves indicate the costs corresponding to the relative proportions of high-risk groups among general practitioners’ patients observed in this study. Impact de la part des patients à risque dans la clientèle des médecins généralistes sur les ratios coût-efficacité différentiels (en euros par test positif) pour chacune des extensions de dépistage du VHC envisagées selon l’hypothèse d’une rémunération de 30 % de consultations supplémentaires. Haute-Normandie, 1997.
a debatable decision. Due to the higher transfusion-related HCV seroprevalence in this population, the effectiveness of screening could be expected to be higher, as was demonstrated by the sensitivity analysis.

The quality of the 3rd generation ELISA used in this study was considered satisfactory; the sensitivity of this test is close to 99% with specificity reported to range from 90% to 99% [4, 23]. This implies a certain number of false positives and false negatives having an impact on cost analysis, a point which requires further study. In addition, the cost of a supplementary consultation to deliver the result of a positive test was not considered. To have a beneficial effect, a positive test implies further explorations and possible treatment, a factor which was not taken into account to assess effectiveness, supplementary cost, or adverse effects [30, 31]. Likewise, the cost to achieve long-term benefit from screening, which implies prevention of cirrhosis and hepatocellular carcinoma, was not considered. The data necessary to examine these factors would require another study to follow-up screened patients or to develop a model which could introduce, for example, the notion of years of life gained [32]. The modelization approach, which can also be used to compare screening strategies based on laboratory and/or clinical findings, is supported by hypothetical assumptions [8, 32, 33] while the present study collected real-life data. No hypothetical assumptions concerning the relative proportion of risk groups among the physician’s patients, patient or practitioner adherence, or prevalence of HCV infection were necessary, except for the sensitivity analysis.

This study was not designed as a general screening program, a most difficult objective [4] whose cost could not be attenuated by an effectiveness only slightly better than a targeted screening program [7]. Our strategies cumulated a small number of factors: blood transfusion before 1991 or at an undetermined date, history of drug abuse, and a third factor. We did not cumulate more than three factors because, in light of the weak effectiveness observed, it was unlikely that adding a fourth factor would improve the results of targeted screening. Strategy $S_2$, addressed a heterogeneous group since it included patients who had a nosocomial occupational risk [34], were former prisoners, or lived with an infected person. These small groups were considered together because in all three, transmission results from close contact with an infected person.

Our findings suggest that extending HCV screening beyond persons with a history of drug abuse or transfusion is not very effective, the extra positive tests inducing a very substantial increase in cost. The highest cost per positive test was observed for strategies defined by target groups with low seroprevalence or representing a large proportion of the consulting patients; the marginal cost-effectiveness ratio for each of these extensions was, in all cases, higher than the median cost of the reference strategy. Extending screening to patients with a history of surgery produced the most extensive strategy studied, nearly corresponding to screening of the general population, an approach considered to be unwarranted [4, 7]. Extending screening to contact with an infected person ($S_5$), a minimally effective strategy with a high marginal cost-effectiveness ratio, would require other arguments to demonstrate that this group of subjects is at risk, although individual tests requested by an exposed person could still be performed. Extension to patients with a history of invasive procedures ($S_3$) was not very effective and rather costly. It must be recalled however that comparing the marginal cost-effectiveness ratio of a given extension with that of the reference strategy is insufficient. All of the studied extensions generated higher costs, but also detected more seropositive patients. Cost must be analyzed not only in terms of strategic effectiveness but also in comparison with overall prevention expenditures. Screening costs must be considered in relation to the threshold, defined by the health insurance fund and the society in general, considered as the limit for screening expenditures for a frequent and serious disease. In this light, extending the screening population to patients with a history of gastroscopy ($S_1$) or colonoscopy ($S_4$) in addition to the reference population ($S_0$) yields a notable gain in effectiveness (+42% and +26% positive tests respectively) at a moderate cost for supplementary screening tests (+2248 € and +2572 € respectively). While it has been demonstrated that endoscopies can be implicated in disease transmission [35, 36], screening patients who underwent endoscopy after 1996, when strict regulatory endoscope disinfection procedures were instituted, would not be warranted, noting also that patients do not always recall the exact date of their endoscopy. These strategies could be retained if new evidence concerning the responsibility of endoscopic procedures in HCV infection becomes available.

Lower cost was naturally noted when expenditure was limited to reimbursement of the screening test (modality $T$). Fixed payment (modalities $F_a$ and $F_b$) was in general more costly than paying for supplementary consultations ($C_{10\%}, C_{30\%}, C_{50\%}$), but could become more attractive for strategies targeting a larger proportion of the consulting patients. The overall and per detected case costs for strategy $S_2$, which targeted about one-half of the patients (42.6%) consulting general practitioners, were lower for the fixed payment modalities ($F_a$ or $F_b$) than for the $C_{30\%}$ modality. Moreover, in the present analysis, screening was limited to one disease. Broadening screening objectives to include several diseases might improve yield.

The screening program analyzed in the present study was designed as a short-term campaign and as such may have introduced a certain degree of selection bias related to seasonal or episodic (epidemic) variations in general practitioner consultations. The network screening campaign conducted in Doubs [37] was much more efficient (5% positive tests) than ours, but the reported cost analysis does not enable a comparison based solely on screening tests performed by general practitioners. Nevertheless, the overall cost of that screening program (administration, screening tests, confirmation tests) was 51 952 € and the cost per detected case was 1 676 €, a level very close to the median cost in our study (1 621 €). This suggests effectiveness would be similar for a much longer period of screening. Furthermore, a prolonged screening campaign raises certain practical problems as was demonstrated in a 15-month study in Ille-de-France [38] where the effectiveness was also better (5% positive tests); unfortunately the lack of an economic analysis prevents comparison.

The general practitioner is a key position for selecting risk groups, delivering information to the patient, and prescribing HCV serology tests. In France, the general practitioner plays a predominant role in targeted screening [39]. Illicit drug users do not constitute a large proportion of patients consulting general practitioners but other screening programs are available for this risk group (prevention centers, associations, post-treatment centers). In a study conducted in Paris, screening effectiveness was better for tests performed at a center for free and anonymous screening than for tests prescribed by general practitioners for patients consulting without an appointment [23]. Conversely, it would be difficult to identify outside the general medicine setting patients transfused before 1994, date at which a transfusion product monitoring system was initiated.

A study of screening strategies based on the experience of health examination centers [40] presented a panel of risk groups for screening similar to those retained for the present study, with one addition concerning a biological parameter (ALAT > 1.2 times the upper normal limit). The seroprevalence in screened patients was very close to that in our population: 119 positive tests out of 9 256 (1.3%) in patients with one or several risk factors as defined by the authors. Similar studies should be performed in other regions and have been advocated by the French Ministry of Employment and Solidarity as part of the national anti-HCV screening and medico-economic evaluation.
campaign [2]. The goal is to better define the role of general medicine and its impact on the HCV-infected population so as to broaden the screening population. It is also noteworthy that, to our knowledge, no data have been published concerning the rate of consultation after an information campaign on risk factors and the importance of screening tests.

In conclusion, this study demonstrated that the reference strategy limiting screening to patients with a history of blood transfusion or drug abuse remains the most efficient approach. Extension of the screening population to other risk groups implies a substantial increase in healthcare costs as well as social consensus for such expenditures.

REFERENCES


