A simplified table using validated diagnostic criteria is effective to improve characterization of colorectal polyps: the CONE CCT teaching program

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ABSTRACT
Introduction and study aims Accurate real-time endoscopic characterization of colorectal polyps is key to choosing the most appropriate treatment. Mastering the currently available classifications is challenging. We used validated criteria for these classifications to create a single table, named CONE CCT, and evaluated the impact of a teaching program based on this tool.

Methods A prospective multicenter study involving GI fellows and attending physicians was conducted. During the first session, each trainee completed a pretest consisting in histological prediction and choice of treatment of 20 colorectal polyps still frames. This was followed by a 30-minute course on the CONE CCT table, before taking a post-test using the same still frames reshuffled. During a second session at 3–6 months, a last test (T3 M) was performed, including these same still frames and 20 new ones.

Results A total 419 participants followed the teaching program between April 2017 and April 2018. The mean proportion of correctly predicted/treated lesions improved significantly from pretest to post-test and to T3 M, from 51.0 % to 74.0 % and to 66.6% respectively (P< 0.001). Between pretest and post-test, 343 (86.6 %) trainees improved, and 153 (75.4 %) at T3 M. Significant improvement occurred for each subtype of polyp for fellows and attending physicians. Between the two sessions, trainees continued to progress in the histology prediction and treatment choice of polyps CONE CCT IIIA. Over-treatment decreased significantly from 30.1 % to 15.5 % at post-test and to 18.5 % at T3 M (P< 0.001).
Introduction

Five subtypes of colorectal polyps have been described: hyperplastic polyps (HP), sessile serrated lesions (SSL), adenomas with a very low risk of undetected adenocarcinoma, adenomas with a high risk of undetected adenocarcinoma and superficial adenocarcinoma (intramucosal or submucosal invasion under 1000 microns (sm1)), and invasive adenocarcinomas (submucosal involvement over 1000 microns).

In theory, therapeutic approach differs according to type of polyp. Whereas HP do not require resection when their diameter is less than 10 mm [1, 2], SSL and adenomas with a very low risk of undetected adenocarcinoma must be completely resected to avoid recurrence, and for these en bloc resection with free margins is preferable but not mandatory. In adenomas with a high risk of undetected adenocarcinoma and superficial adenocarcinomas, endoscopic biopsies (EPMR), as it allows proper pathological assessment and avoids local recurrence, despite this being associated with higher risk of complication [3]. For invasive adenocarcinomas, surgery with lymphadenectomy and/or chemotherapy but with higher risk of complication [3]. For invasive adenocarcinoma (type 3) from adenomas and superficial carcinoma (type 2). This classification does not differentiate between adenomas with a very low risk of undetected adenocarcinoma and those with a high risk of undetected adenocarcinoma and superficial adenocarcinomas, although their treatment responds to different constraints. The JNET Classification [8] differentiates low-risk adenomas from superficial invasive carcinoma with a good accuracy (77.1% for type 2A and 78.1% for type 2B). However, it does not take into account the macroscopic type of laterally spreading tumors, in which invasive adenocarcinoma may exist despite the lack of an irregular pattern, as demonstrated by Yamada et al. (21.1% for LST NG, 15.0% for LST G with large nodule or depression) [11]. The SSLs are only described in WASP classification with a good accuracy [10].

We therefore merged criteria for these seven validated classifications into a single table named Colorectal Neoplasia Endoscopic Classification to Choose the Treatment (CONECCT; ✶ Fig. 1) with a pragmatic proposal of the most appropriate treatment based on each subtype of colorectal polyp and on the European Society of Gastrointestinal Endoscopy guidelines (ESGE) [3, 12]. The current study aimed to assess the impact of a teaching program, using this newly created table, in terms of accuracy of polyp characterization, and choice of appropriate treatment.

Methods

Design

We conducted a prospective multicenter study including trainees (gastroenterology fellows and attending physicians) who were evaluated before, and immediately and at 3 to 6 months after a teaching course on characterization and treatment of colorectal lesions using the CONECCT table.

CONECCT table

The CONECCT table was created using a combination of criteria used in the aforementioned classifications (Paris4, LST5, NICE7, Kudo6, WASP10, JNET8, Sano9), by physicians from the research and development committee of the Société Française d’Endoscopie Digestive (SFED; ✶ Fig. 1). Characterization of the lesions was based on the macroscopic aspect, the color on narrow band imaging (NBI), vascular pattern and pit pattern. To characterize a polyp using the CONECCT table, at least two imaging conditions are required. On the one hand, a white-light distant image of the polyp is required to analyze its macroscopic aspect. On the other hand, a virtual chromoendoscopy-ready image with magnification, if possible, is needed to analyze the microscopic structures of the polyps and identify diagnostic criteria associated with a risk of neoplasia. For each subtype of colorectal polyp, this table suggested a treatment, based on the latest guidelines from the ESGE [3, 12].

HP (CONECCT IH) are mostly seen in the rectum and the sigmoid. These lesions have the following features based on the NICE classification [7]: color is same or lighter than background, vessels are lacking or isolated lacy vessels coursing across the lesion that do not surround the pits and the surface pattern has dark or white spots of uniform size or homogeneous absence of pattern. IH are usually small and numerous. Risk of progression to cancer is null and guidelines do not recommend resection of these polyps after proper identification.

Conclusion

The CONECCT teaching program is effective to improve the histology prediction and the treatment choice by gastroenterologists, for each subtype of colorectal polyp.
using virtual chromoendoscopy (NBI) if they are less than 5 mm [12].

SSLs (CONECT IS) are characterized using the WASP classification [10], two of the following criteria are required: indistinctive border, clouded surface, irregular shape and dark spots inside the crypts. SSL are frequently covered by a yellowish mucus cap, and although not used in the WASP classification [10] as a diagnostic criterion, this was added to the table to aid recognition. For SSL, resection is recommended given the risk of cancer (via \textit{BRAF} mutation). However, most of these lesions are not dysplastic and reports of transformed SSL are rare. Thus, low-risk endoscopic resection methods without aiming for completely free margins are recommended (preferably En Bloc) to reduce the risk of perforation [12].

Adenomas with a high risk of undetected adenocarcinoma and superficial adenocarcinomas (CONECT IIC) constitute the fourth subtype of colorectal polyp. Adenomas with a high risk of undetected adenocarcinoma are lesions without clear evidence of adenocarcinoma, but with a high risk of invasive carcinoma because of their macroscopic aspect. Non-granular LST (LST NG) and LST G with large nodules (>1 cm) for instance have a high risk of invasive carcinoma, over 15% [5]. Given this risk, en bloc resection is recommended, as this allows correct pathological examination that, in turn, avoids underestimation of the depth of invasion. Superficial adenocarcinomas are lesions with evidence of neoplasia but no clear features of deep submucosal invasion. For instance, a slightly depressed lesion (Paris classification IIc) [4], the lake of uniformity of the vessels and the high

<table>
<thead>
<tr>
<th>CONECC</th>
<th>IH hyperplastic</th>
<th>IS sessile serrated lesions</th>
<th>IIA adenoma</th>
<th>IIC high risk adenoma or superficial adenocarcinoma</th>
<th>III deep invasive adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macro</td>
<td>Often small &lt; 10 mm aspect IIa Paris</td>
<td>Paris Ila or Ilb plateau aspect, unclear margins</td>
<td>Paris Ip, Is or Ila rarely depressed</td>
<td>Often Iic ou IIc + Iic or LST non granular or macronodule (&gt; 1 cm) on granular LST</td>
<td>Often III or Iic with nodule in the depression spontaneous bleeding</td>
</tr>
<tr>
<td>Color (NBI)</td>
<td>Clear or equivalent to background</td>
<td>Variable yellow mucus (red with NBI)</td>
<td>Darker than background</td>
<td>Often dark</td>
<td>Heterogenous, dark or clear in amorphous area</td>
</tr>
<tr>
<td>Vessels (NBI or equivalent)</td>
<td>Lack of visible vessels or thin vessels across the lesion not following pits</td>
<td>Sometimes absent dark spots in the bottom of pits</td>
<td>Regular following pits</td>
<td>Irregular but persisting no avascular area</td>
<td>Irregular large interrupted vessels or absent vessels (avascular areas)</td>
</tr>
<tr>
<td>Pits (chromoendoscopy real or virtual)</td>
<td>Round shape whitish pits</td>
<td>Round shape dark dots (NBI)</td>
<td>Elongated or branched crypts, cerebriform aspect</td>
<td>Irregular but maintained no amorphous area</td>
<td>Absent, amorphous destroyed or irregular (clear demarcation)</td>
</tr>
<tr>
<td>Resection proposed</td>
<td>No resection</td>
<td>En bloc R0 if possible but piece meal ok</td>
<td>En bloc R0 (EMR or ESD if &gt;20 mm)</td>
<td>Surgery with lymphadenectomy</td>
<td></td>
</tr>
</tbody>
</table>

![Fig.1 CONECC table. The words in bold are the ones that require particular attention when analyzing lesions.](image)
density of capillary vessels without avascular areas (Sano’s IIIa) [9] or presence of an irregular pit pattern (irregular mucosal pattern without any amorphous area and without demarcation line; Kudo’s type V) [6] are associated with a high risk of invasive components and should be resected en bloc with free margins, to allow pathological examination and curative resection [12]. Irregular mucosal and vascular pattern also define type 2B of the JNET classification [8].

Invasive adenocarcinomas (CONECCT III) typically presents with features associated with a high risk of deep submucosal invasion such as an excavated shape (Paris III classification [4]), nodule or pseudo mass within a depressed LST NG, avascular areas (Sano’s IIIb) [9] loss or decrease of pits with an amorphous structure (Kudo Vn) or an irregular pit pattern in a demarcated area (Vi invasive) [6]. These avascular and amorphous features are also used in the NICE (type 3) and JNET classifications (type 3) [8]. In such cases, endoscopic procedures are not indicated. Patients must be referred to an oncologist.

**Trainees and teaching program**

Fellows from the seven French districts (Paris region, Northwest, Northeast, Southwest, Southeast, West, and East) were invited to participate in the study as ‘trainees’ after signed consent. In France, gastroenterology fellows are postgraduate (post-medical school) students specializing in hepatology, gastroenterology, and endoscopy. Attending physicians were also invited to participate by the French society of digestive endoscopy (Société Française d’Endoscopie Digestive – SFED), via email, newsletter, website publications, and during nationwide meetings.

Teaching program was divided into two training sessions occurring at least 3 months apart (this design was chosen for feasibility reasons as well since gastroenterology fellows in France are available all together only twice a year). Each trainee created an identification number (ID) from his/her initials and date of birth. For each training session, the trainee was requested to indicate his/her ID on the reply form to match their identity with the test answers. Trainees were excluded from the first training session if they did not complete each of the two required tests (pretest and post-test) in the first training session, and from the second training session analysis at 3 to 6 months (T3 M) if their ID could not be matched with that used in the first training session.

For each training session, the different tests (pretest, post-test, and T3 M) were taken either in person on paper or online (Google Forms, Google Inc., California, United States). Images of the lesions were projected by a video projector if the training session was done in a classroom, otherwise they appeared on their computer screen if the participant answered online. Participants had as much time as they wanted to analyze the images.

**First training session**

The first training session was divided into five steps:

- **Step 1**: Evaluation of awareness and clinical use of the seven classifications used in the CONECCCT table (Paris [4], LST [5], NICE [7], Kudo [6], WASP [10], JNET [8], Sano [9]).

- **Step 2 (pre-test)**: Histological prediction and treatment choice for 20 colorectal polyps. To predict histology, trainees were provided with one to five images per lesion, at least one of which was taken with NBI, the rest being taken in WL; lesions were not dyed. The location in the colon of the polyps were provided.

- **Step 3**: Standardized 30-minute teaching course given by French endoscopy experts (endoscopists currently performing advanced endoscopic diagnosis and ESD) from the research and development committee of the SFED and describing the content of the CONECCCT table, including the criteria for each of the five subtypes of colorectal polyps with several examples, as well as the recommended treatments.

- **Step 4 (post-test)**: Identical to pretest, but frames in a different order. Of note, regarding histological prediction, trainees had to reply using the CONECCCT table that was provided to them. For both tests, the breakdown of lesions was as follows: three HP, four SSLs, five adenomas, four high-risk adenoma or superficial adenocarcinomas and four deep invasive adenocarcinomas.

- **Step 5**: At the end of the first training session, the group of trainees were informed of the correct histological prediction and the treatment choice for each example but did not receive individual feedback as to potential errors.

**Second training session (T3 M)**

Three to 6 months after the first training session, the trainees took the T3 M test that consisted of still frames depicting a total of 40 colorectal polyps, including the 20 polyps used during the first training session and 20 new polyps. The questions were identical to those in the first training session and there was no additional teaching course. The breakdown of lesions was as follows: seven HP, eight SSLs, nine adenomas, eight high-risk adenomas or superficial adenocarcinomas and eight deep invasive adenocarcinomas.

**Evaluation of the trainees’ answers**

For each individual frame, the answer was considered correct if the trainee chose the correct histological prediction or treatment choice. Regarding histological prediction, trainees chose among the following possibilities: HP, SSL, adenomas with a very low risk of undetected adenocarcinoma, adenomas with a high risk of undetected adenocarcinoma and superficial adenocarcinomas and deep invasive adenocarcinomas. The correct histological prediction was defined by the histology report from a group of pathologists with expertise in digestive histology for HP (CONECCT IIT), SSL (CONECCT IS), and deep invasive adenocarcinoma (CONECCT III). To differentiate adenomas with a very low risk of undetected adenocarcinoma (CONECCT IIA) from adenomas with a high risk of undetected adenocarcinoma and superficial adenocarcinomas (CONECCT IIC), the correct histological prediction was defined by an expert group of endoscopists from the SFED (JR, MP, JJ) who arrived at a consensus using the Delphi process, and for adenomas histology was used to detect presence of adenocarcinoma and therefore distinguish between risk of undetected adenocarcinoma. All resection pieces were fixed in buffered formalin and then embed-
ded in paraffin before being cut into 2-mm slices. Regarding treatment choice, trainees chose among the following: no resection, resection (preferably en bloc, but piecemeal acceptable), resection en bloc with free margins (R0) and surgery with lymphadenectomy. The correct treatment choice was in accordance with ESGE guidelines for each type of lesion. Over-treated lesions were defined as those for which a more invasive treatment than necessary was proposed and undertreated lesions as those for which a less invasive treatment than necessary was proposed.

Correctly predicted/treated lesions were those for which trainees chose both the correct histological prediction and treatment choice. At 3 to 6 months, trainees were also asked if they had used the CONECCCT table on a daily basis since the first training session, and if they considered CONECCCT useful for histological prediction and treatment choice in their routine practice.

Endpoints
The endpoints were:
- histological prediction, treatment choice, and the mean of correctly predicted/treated lesions between pretest (step 2) and post-test (step 4), as well as between the first training session (pre-test and post-test) and the second training session 3 to 6 months later (T3M)

- Comparison between gastroenterology fellows and attending physicians

- Overall number of overtreated, undertreated lesions, and unnecessary surgeries

- Analysis by histological subtype (test results, over and undertreated)

Statistical analysis
Baseline characteristics and outcome variables were described by the mean and range for continuous variables, and by frequencies and percentages for categorical ones. Comparisons of proportions between time points were performed using a mixed logistic regression model to take into account the fact that an investigator classified multiple lesions, and that lesions were classified at different time points. Comparisons of proportions between investigators (fellows and attending physicians) were also performed by mixed logistic regression models to take into account the fact that the same investigator classified multiple lesions. P<0.05 was considered statistically significant. All analyses were performed using Excel software (Office, Microsoft, United States) or the R software (R Core Team 2018: R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.)

Ethical concerns
All trainees received oral information about the study protocol and signed a written consent for participation. The protocol followed the declaration of Helsinki and was approved by the local ethics committee (Comité d’éthique du Centre Hospitalo-Universitaire de Lyon).

Registration
The study was registered in the US National Clinical trial register under the number NCT03455595.

Results
All training sessions took place between April 2017 and April 2018. A total of 419 gastroenterology fellows and attending physicians participated in the first training session; 23 were excluded because they had not performed the post-test, and therefore 396 trainees were analyzed (275 GI fellows, 121 attending physicians; Fig. 2).

A total of 302 gastroenterology fellows and attending physicians participated in the second training session; 99 were excluded because of ID matching issues (n = 96, either a failure to complete the ID or a change in the ID) or because the post-test during the first training session had not been performed (n = 3), and therefore 203 trainees were analyzed (137 GI fellows, 66 attending physicians; Fig. 2). Mean ± SD age of the gastroenterology fellows was 26.9 ± 1.9 years, and that of attending physicians 43.8 ± 11.9 years.

First training session, step 1 results
The Paris classification was used by 63.4% of trainees, 28.5% used the NICE classification, 36.8% used the Kudo classification, 10.9% used the Sano classification, and 7.6% used the WASP classification. Overall, 1.5% of the fellows and 9.9% of the attending physicians used all classifications while 13.2% used any of them.

Results in the first training session (pretest and post-test)
At post-test compared to pretest, there was a statistically significant improvement in the mean proportion of correct histological prediction, from 60.5 to 76.2 % (+ 26.4 %, P<0.001), and correct treatment choice, from 61.1 to 77.4 % (+ 26.8 %, P<0.001). Mean proportion of correctly predicted/treated lesions improved statistically significantly, from 51.0 % to 74.0 % (+ 45.1 %, P<0.001). Trainees improved their performances between pretest and post-test in 86.6 % of cases (343/396).

The pretest results of the attending physicians were statistically significantly better than those of gastroenterology fellows (73.9 % vs. 54.6 % for the histological prediction, 69.9 % vs. 57.2 % for the treatment choice, both P<0.001). Mean improvement in post-test results for gastroenterology fellows was statistically significantly higher than that for attending physicians (+ 34.8 % vs. + 11.1 % for the histological prediction, 31.6 % vs. 17.9 % for the treatment choice, both P<0.001; Table 1).

Results in the second training session (T3M)
At T3M compared to pretest, there was a statistically significant improvement in mean proportion of correct histological prediction, from 60.5 to 70.3 % (+ 16.2 %, P<0.001), and correct treatment choice, from 61.1 to 70.9 % (+ 16.0 %, P<0.001). The mean proportion of correctly predicted/treated lesions improved statistically significantly, from 51.0 % (4040/
Trainees improved their performances between pretest and T3M in 75.4% of cases (153/203).

Mean proportion of correct answers for fellows and attending physicians were 73.6% and 82.1% for histological prediction, respectively, and 75.3% and 82.4% for treatment choice, respectively. Compared to the pretest results, a statistically significant difference in favor of the T3M was seen for the fellows (+34.8%, both with \( P < 0.001 \)) and for the attending physicians (+11.1% and +17.9%, both with \( P < 0.001 \)).

Decrease in the mean proportion of correctly predicted/treated lesions between the end of the first training session (post-test) and the second training session (T3M) was more pronounced for the fellows than for the attending physicians (−17.3% for the fellows vs −1.3% for the attending physicians, \( P < 0.001 \); ▶ Table 1).

### Overall number of over and undertreated lesions and unnecessary surgeries

At post-test compared to pretest, there was a statistically significant reduction in the number of overtreated lesions, from 30.1% (2383/7920) to 15.5% (1227/7920; −48.8%, \( P < 0.001 \)) and in the number of undertreated lesions, from 8.0% (633/7920) to 6.7% (530/7920; −16.3%, \( P < 0.001 \)). Also, colorectal lesions were statistically significantly more overtreated than undertreated (30.1 vs 8.0%, \( P < 0.001 \)).

At T3M compared to pretest, there was a statistically significant reduction in the number of overtreated lesions, from 30.1% (683/7920) at post-test to 6.3% (496/7920) at post-test (−27.4%, \( P < 0.001 \)).

The number of unnecessary surgeries was statistically significantly reduced, from 8.6% (683/7920) at post-test to 5.7% (467/8120) at T3M (−33.7%, \( P < 0.001 \)).

### Analysis by polyp subtype

Regarding lesions CONECCIT I, mean proportion of correctly predicted/treated lesions was 62.0% at pretest, 93.7% at post-test and 73.7% at T3M. The differences were statistically significant between pretest and post-test (\( P < 0.001 \)), pretest and T3M (\( P < 0.001 \)) and post-test and T3M (\( P < 0.001 \)). Mean proportion of overtreated lesions were 35.9% at pretest, 5.5% at post-test and 25.2% at T3M. Differences were statistically significant between pretest and post-test (\( P < 0.001 \)), pretest and T3M (\( P < 0.001 \)) and post-test and T3M (\( P < 0.001 \)).

Regarding lesions CONECCIT IS, mean proportion of correctly predicted/treated lesions were 33.4% at pretest, 71.1% at post-test and 58.6% at T3M. Differences were statistically significant between pretest and post-test (\( P < 0.001 \)), pretest and T3M (\( P < 0.001 \)) and post-test and T3M (\( P < 0.001 \)). Mean proportion of overtreated lesions were 45.5% at pretest, 22.1% at post-test and 30.6% at T3M. Differences were statistically significant between pretest and post-test (\( P < 0.001 \)), pretest and T3M (\( P < 0.001 \)) and post-test and T3M (\( P < 0.05 \)).

Regarding lesions CONECCIT IIA, mean proportion of correctly predicted/treated lesions were 42.8% at pretest, 67.7% at...
Fig. 3  Mean proportion of correctly predicted/treated lesions by subtype of polyp.

Fig. 4  Mean proportion of overtreated lesions by subtype of polyp.
post-test and 70.1% at T3 M. Differences were statistically significant between pretest and post-test (P<0.001), pretest and T3 M (P<0.001) and post-test and T3 M (P<0.001; ▶ Fig. 3).

Mean proportion of overtreated lesions were 36.5% at pretest, 23.0% at post-test and 18.5% at T3 M. Differences were statistically significant between pretest and post-test (P<0.001), pretest and T3 M (P<0.001) and post-test and T3 M (P<0.001; ▶ Fig. 4).

Mean proportion of undertreated lesions was 3.5% at pretest, 1.7% at post-test and 2.5% at T3 M. Differences were statistically significant between pretest and post-test (P<0.001) and between pretest and T3 M (P<0.01; ▶ Fig. 5).

Regarding lesions CONECCCT IIC, mean proportion of correctly predicted/treated lesions were 42.8% at pretest, 57.6% at post-test and 52.2% at T3 M. Difference were statistically significant between pretest and post-test (P<0.001), pretest and T3 M (P<0.001) and post-test and T3 M (P<0.01; ▶ Fig. 3).

Mean proportion of overtreated lesions were 32.4% at pretest, 22.5% at post-test and 18.6% at T3 M. Differences were statistically significant between pretest and post-test (P<0.001), pretest and T3 M (P<0.001) and post-test and T3 M (P<0.01; ▶ Fig. 4).

Mean proportion of undertreated lesions was 16.0% at pretest, 17.2% at post-test and 25.3% at T3 M. Differences were not statistically significant (▶ Fig. 5).

Regarding lesions CONECCCT III, mean proportion of correctly predicted/treated lesions were 80.3% at pretest, 86.6% at post-test and 78.8% at T3 M. Differences were only statistically significant between pretest and post-test (P<0.001; ▶ Fig. 3).

Mean proportion of undertreated lesions were 15.9% at pretest, 12.2% at post-test and 17.2% at T3 M. Difference was only statistically significant between pretest and post-test (P<0.001; ▶ Fig. 5).

Value of the CONECCCT TABLE
At T3 M, 87.0% of the trainees considered the CONECCCT table to be a useful tool to predict histology of a colorectal polyp, and 89.0% for choosing a treatment. At T3 M, 40.3% of trainees routinely used CONECCCT.

Discussion
The current study found that a teaching program of the CONECCCT table is effective in improving histological prediction and treatment choice for colorectal polyps in both fellows and attending physicians specializing in gastroenterology. The benefits of this program were found regardless of the type of lesion and personal experience. In clinical practice, this improvement yielded a reduction of under- and overtreatment of colorectal polyps and could thus potentially impact treatment of these lesions. Furthermore, there was a persistent statistically significant improvement after 3 to 6 months.

For each subtype of polyps, there was a statistically significant improvement between pretest and post-test in histological prediction and treatment choice. These results are encouraging, particularly for CONECCCT IH lesions, because the minimal
In conclusion, the CONECC teaching program is effective in improving histological prediction and treatment choice performance, regardless of the type of colorectal polyp considered, and for both gastroenterology fellows and attending physicians. Despite these encouraging results, further sessions are needed to maintain or improve the level of participants. A validation study for this table is currently underway.

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Competing interests

None

References


