FACTORS INHIBITING THE IMPLEMENTATION OF THE ATRAUMATIC RESTORATIVE TREATMENT APPROACH IN PUBLIC ORAL HEALTH SERVICES IN GAUTENG PROVINCE, SOUTH AFRICA

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ABSTRACT

Objective: To investigate potential barriers to the utilisation of the ART approach in a South African public oral health service. Method: 7 barriers were identified: patient load/work load, operator opinion, patient opinion, service management, material supply, clinical ART skill, chair-side assistance. Operators were asked to answer a questionnaire one year after completing the ART training. Responses ranged from 1 = no barrier to 5 = highest barrier. Treatment data per operator were collected during 1 year after training, for both dentitions, including: number of extracted teeth, placed traditional restorations, ART restorations. The restoration/extraction (REX) ratio and the proportion of ART restorations (ART%) of the total number of restorations were calculated and correlated with the barrier variables. Pearson correlation, ANOVA and 2-tailed t-tests were used in the statistical analyses. Results: Patient load/work load (mean = 2.80; SE = 0.16) was the strongest barrier (p<0.001) and clinical ART skill was the weakest barrier (p<0.001). A significant correlation between material supply and mean REX score was observed in both dentitions. In primary teeth, the ART% correlated significantly with clinical ART skill (r= -0.63; p<0.01). In permanent teeth, statistically significant correlations were observed between ART% and patient load/work load (r = -0.54; p<0.05), patient opinion (r = -0.76; p<0.01), operator opinion (r = -0.53; p<0.05), chair-side assistance (r = -0.57; p<0.05), oral health service management (r = -0.46; p<0.05). Conclusions: 1 year after ART training completion high patient load/work load, followed by insufficient provision of materials/instruments, were the two most inhibiting barriers to the use of ART in the public oral health services. Dentists’ perceptions of low clinical skill levels in performing ART confidently inhibited the use of ART in primary teeth in children.

Uniterms: Atraumatic restorative treatment; Treatment barriers; Public oral health services; South Africa; Dental education.

INTRODUCTION

Atraumatic Restorative Treatment (ART) is based on the removal of soft denaturated carious tooth tissue using hand instruments only. In most cases, the cleaned cavity is then conditioned and restored with a high-viscosity glass ionomer cement. The ART approach evolved in response to the unavailability of restorative care in population groups with limited resources. Owing to its independence from electricity and expensive dental equipment, ART appears to offer a pragmatic solution to the problems related to restoring tooth cavities and sealing caries-prone tooth surfaces that oral health workers face in developing countries. Makoni, et al. (1997) showed that ART could be applied in 84% of dental lesions in a population with a caries prevalence of 41% and a mean DMFT score of 1.1. Based on a meta-analysis, Frencken, et al. (2004) reported that no difference existed between survival results of single-surface ART restorations and comparable amalgam restorations in the permanent dentition after 3 years. Recently, the survival percentage after 6.3 years, of ART restorations using glass ionomer, was reported to be higher than that of comparable restorations placed through the traditional approach using amalgam.

ART was officially adopted by the World Health Organisation (WHO) in 1994 as a suitable caries-controlling...
approach for use in primary oral health care programmes in developing countries13. Reports from developing countries such as South Africa, The Gambia and Uganda have recommended the use of ART for addressing the need and demand for preventive and restorative care in their countries1,2,19.

As in other developing countries, the public oral health service in South Africa is characterised by limited financial resources, a resulting critical shortage of oral health personnel and inadequate facilities to cope with the increasing level of oral disease and demand for treatment24. In South Africa, only 11% of all dentists work in the public dental service, mostly in urban centres33, whereas 80% of the population relies on the public health services for oral care and only 73% live in urban areas12,20,29. The shortage of oral health personnel, inaccessibility of oral health services and low priority of oral health amongst members of the communities have been identified as barriers to obtaining oral care24. The low priority given to oral health by many people is considered to be related to prevailing ignorance about disease prevention. As a result of this, many patients use dental services mainly for symptomatic reasons, such as toothache31, seeking tooth extraction rather than restoration to treat painful cavitated dental lesion30.

In line with the endorsement and recommendation from WHO32, ART was introduced into South African public oral health services in 1998, in an attempt to improve the oral health services through changing the carries treatment pattern from predominantly extracting, to restoring teeth. A study was set up in 2001, in which 21 dentists working in the regional public service of Ekurhuleni, Gauteng Province, were trained in ART during a 3-day course. Evaluation after one year showed that each of these dentists had placed, on average, 5 ART restorations per month, compared to an average of 19 traditional restorations. This finding was unexpected. The expectation had been that a higher number of ART restorations would result after dentists had attended preventive services. They accepted that a visit to a dentist was needed only when one had toothache and that tooth extraction was the sole treatment to be provided. Furthermore, owing to the scarcity of dental clinics in rural and periurban areas, patients have to travel long distances. Because of the high number of patients seeking dental care, many have to wait long hours before being attended to. As most of these patients are poor, costs of travel to the dental clinics are considered to be very high. For these reasons, most patients report for dental treatment at a stage when tooth extraction is usually the only possible treatment left. In addition, many patients may prefer the removal of a decayed tooth to restoration of the cavity, as the latter may need to be repaired later and thus require an additional visit to the clinic, costing time and money. For the same reason, patients may refuse restorative treatment of carious teeth diagnosed during a visit to the dentist for an extraction, regarding them as unproblematic.

- 4. Oral health service management - A lack of resources may lead to insufficiencies in oral health care management. Inefficient management may lead to a lack of operator guidance and leadership with respect to the implementation of new treatment methods, such as those used in the ART approach. After having accepted a new method, health authorities should include the method into its list of standards-of-care, providing treatment guidelines and targets, and monitoring implementation. Without such

MATERIAL AND METHODS

Ethical clearance for the main study was obtained from the Ethics Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand, Johannesburg, South Africa under protocol number M00/07/13.

All 21 dental operators employed full-time in the Ekurhuleni region in Gauteng Province had been trained in ART in 2001. The training followed recommended course standards1 and was conducted by a staff member (SM) of the Division of Public Oral Health, University of the Witwatersrand, Johannesburg.

Description of identified barriers

Seven factors related to the provision of service were identified as possibly exercising an inhibitory influence (barrier effect) on the utilisation of ART by dental operators in public health services in South Africa16. These were: patient load / work load, operator opinion, patient opinion, oral health service management, material supply, clinical ART skill, chair-side assistance.

- 1. Patient load / work load - Extraction as a useful method of addressing a high load of patients requiring pain relief was considered one of the main inhibitors to provision of restorative care. It has been established that extracting teeth requires on average 7 min. and restoring teeth (including ART), between 15 and 20 min21. Patients’ demands for pain relief through extraction do influence operator choice in relation to using restorative treatment of tooth cavities.

- 2. Operator opinion - A general lack of motivation and a negative opinion amongst operators concerning the adoption of new treatment methods may result in resistance to using new clinical procedures such as ART22.

- 3. Patient opinion – Under the previous political system in South Africa the delivery of well-organized oral care was restricted to a small percentage of the population. The large majority were not introduced to oral health promotion and preventive services. They accepted that a visit to a dentist was needed only when one had toothache and that tooth extraction was the sole treatment to be provided. Furthermore, owing to the scarcity of dental clinics in rural and periurban areas, patients have to travel long distances. Because of the high number of patients seeking dental care, many have to wait long hours before being attended to. As most of these patients are poor, costs of travel to the dental clinics are considered to be very high. For these reasons, most patients report for dental treatment at a stage when tooth extraction is usually the only possible treatment left. In addition, many patients may prefer the removal of a decayed tooth to restoration of the cavity, as the latter may need to be repaired later and thus require an additional visit to the clinic, costing time and money. For the same reason, patients may refuse restorative treatment of carious teeth diagnosed during a visit to the dentist for an extraction, regarding them as unproblematic.
guidance operators may think that the authorities are not serious about the new method and ignore it in their daily practice.

- 5. Material supply - Late or irregular supplies cause shortages of materials and instruments necessary to provide a treatment. Introducing a new treatment method often goes hand-in-hand with the necessity to order new materials and instruments. If ordering and supplying is not well organised, a new treatment method will have a difficult start; for example, a high-viscosity glass ionomer, that may not be available in the clinic at first, is needed for ART.

- 6. Clinical ART skill - It is recognized that ART, like traditional restoration, can fail because of operator-related factors. Insufficient skills and/or diligence in performing ART will lead to restoration failures that, in turn, may generate a negative feedback which may result in reduced motivation of the operator to continue applying the ART approach instead of resorting to well-known traditional treatment methods.

- 7. Chair-side assistance - A lack of effective chair-side assistance results in operators’ having to perform assisting functions such as mixing filling material themselves. This would increase the operator time required for treating patients and, in order to avoid that situation, lead them to resort to less time-consuming procedures, such as using rotating instruments.

Evaluation

In order to evaluate the barriers identified, a 30-item questionnaire was developed and piloted (Table 1). One year after completion of the ART training operators were asked to fill in the questionnaire using the 5-point Likert scale. A trained field worker distributed and collected the questionnaire. In order to quantify the value of each barrier, responses were ranged from 1 = no barrier to 5 = highest barrier. For each operator, dental treatment records; including the number of extracted teeth, number of restorations placed through the traditional and ART approach for both the primary and permanent dentition, were collected over a one year period after completion of the ART training (August 2001 – July 2002).

Statistical analysis

The analysis was done by a biostatistician (MvH). Based on the collected statistics, the restoration/extraction (REX) ratio and the proportion of ART restorations to the total number of restorations per operator were calculated and correlated with the barrier variables, using the Pearson correlation coefficient. In the same way the barrier variables were correlated with each other. Differences between the mean barrier values were tested using ANOVA and the 2-tailed t-test. Statistical significance was set at the 5% level. The overall Cronbach’s alpha for the questionnaire was 0.7, indicating a high reliability level in the data obtained.

RESULTS

Operator information

Two operators did not complete the questionnaire and were excluded from the analysis. Of the remaining nineteen dental operators, 58% were female and 42% were male. Their mean age was 39.8 (SD = 9.6) years; mean number of years graduated, 14.3 (SD = 9.8) years; mean number of years spent working at the clinic in Ekurhuleni, 10.3 (SD = 8.3).

Oral treatment

The mean number of patients treated per day by each operator was 26 (SD = 8). Tooth extraction was the most frequently performed treatment (Table 2). Most of the restorations were placed using the traditional approach under local anaesthetics. The mean numbers of traditional restorations in permanent and primary teeth per operator were 190 (SD = 313) and 18 (SD = 28), respectively. ART restorations were the main type of restoration placed in the primary dentition. On average, each operator had used the ART approach to place 72% of all restorations in primary teeth and 20% of all restorations in permanent teeth.

Barriers to implementing the ART approach

One operator did not respond to the questions about patient load and operator opinion.

The barrier factor patient load/work load had the highest mean value: 2.80 (SE = 0.16), whereas clinical ART skill scored lowest; 0.47 (SE=0.14). A statistically significant difference existed between the mean score of the barrier factor, patient load/work load, and the mean scores of the other barrier factors (ANOVA; t-test p<0.001). The mean score of the barrier factor, clinical ART skill, was statistically significantly different from the mean scores of all the other barrier factors (ANOVA; t-test p<0.001). Figure 1 shows a box-plot of the barriers under study.

A significant correlation between material supply and the mean REX score in primary dentitions (r = 0.49; p<0.05) and in permanent dentitions (r = 0.48; p<0.05) was observed (Table 3). In primary dentitions, the proportion of ART restorations correlated significantly with clinical ART skill (r = -0.63; p<0.01). In permanent dentitions, statistically significant correlations were observed between the proportion of ART restorations and the barrier factors patient load/work load (r = -0.54; p<0.05), operator opinion (r = -0.76; p<0.01), operator opinion (r = -0.53; p<0.05), chair-side assistance (r = -0.57; p<0.05) and oral health service management (r = -0.46; p=0.05).

Correlations among all barrier factors are shown in Table 4. Statistically significant correlations were observed between patient load/work load and operator opinion (r = 0.70; p<0.05) and between patient load/work load and patient opinion (r = 0.73; p<0.01). There was a significant correlation between the barrier factors, operator opinion and patient opinion (r = 0.77; p<0.01). The barrier factors, oral health service management, correlated significantly with operator opinion (r = 0.52; p<0.05) and patient opinion (r = 0.57; p<0.01).
DISCUSSION

This study assessed the effect of possible barriers upon the low level of utilisation of the ART approach observed in a regional public oral health service system of South Africa. In the data analysis a common phenomenon that warrants discussion was encountered. ANOVA should be used when the means of three or more groups need to be compared. However, a prerequisite is the need for a near to equal variance of the group variables. This was not entirely the case in 3 of the 7 factors in the present study. However, the fact that the use of ANOVA indicated a very strong difference (p<0.001) between the groups shows that the barrier factors, *patient load/work load* and *clinical ART skill*, indeed differed significantly from the other barrier factors, although the real level of significance would have been somewhat higher. In order to ensure a true difference between the *patient load/work load* and *clinical ART skill* barriers and the remaining barriers, the t-test was applied. The mean score of *patient load/work load* was compared to that of the next highest mean score (*material supply*), and the mean score of *clinical ART skill* was compared to that of the next lowest mean score (*patient opinion*). Both comparisons yielded a highly statistically significant difference (p<0.001). Obviously, this was not the case in 3 of the 7 factors in the present study.

**TABLE 1-** Questionnaire used to assess possible barrier factors

<table>
<thead>
<tr>
<th>Item</th>
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</table>
| **General** | Type of operator occupation and place of clinic  
Operator age  
Operator gender  
Year of graduation of operator  
School where operator has graduated  
Years working in present clinic |
| **Barrier factors** | Operators were asked to indicate whether they “strongly agree”, “agree”, are “undecided”, “disagree” or “strongly disagree” with the following statements: |
| **1. Patient load / work load** | I have to treat too many patients during the day  
I have no time to do ART in my clinic  
ART fillings take longer to do than amalgam or composite fillings. |
| **2. Operator opinion** | I have attended the ART course and I find applying ART in the public clinic an effective service for patients  
When I do fillings, I prefer to use the drill, because I find it easier  
I consider ART an inferior treatment option as compared with other restorations  
I feel a sense of accomplishment when I am able to restore a tooth  
I feel better when I do not have to give a local anaesthetic.  
I feel a sense of accomplishment when I do not have to drill when preparing a cavity  
I prefer to use the drill because it is much quicker  
I prefer to use the drill because it is better  
I would like to spend more time rendering ART in my clinic |
| **3. Patient opinion** | In my clinic, patients prefer tooth extraction to restorations  
In my clinic, patients prefer ART to other tooth restorations  
My patients are very grateful and satisfied, if I restore their teeth using the ART technique.  
My patients are very grateful and satisfied, when I don’t have to inject them.  
My patients are very grateful and satisfied, when I don’t have to drill their teeth |
| **4. Oral health service management** | My clinic manager fully understands the concept of ART  
My clinic manager fully supports ART in our clinic |
| **5. Material supply** | I have a constant and adequate supply of ART materials to my clinic  
I have sufficient instruments available in my clinic, in order to render ART |
| **6. Clinical ART skill** | I have had adequate training, in order for me to feel confident when rendering ART  
I would like to have more training in the theoretical aspect of ART |
| **7. Chair-side assistance** | My chairside assistant is skilled to assist me in rendering ART |
TABLE 2- Mean scores and Standard Deviation (SD) of treatments provided per operator and per dentition during a 12 months post ART training period

<table>
<thead>
<tr>
<th>Type of treatments</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ex extractions</td>
<td>474</td>
<td>244</td>
</tr>
<tr>
<td>Non-ART restorations</td>
<td>18</td>
<td>28</td>
</tr>
<tr>
<td>ART restorations</td>
<td>39</td>
<td>58</td>
</tr>
<tr>
<td>Restoration - Extraction ratio (REX)</td>
<td>0.17</td>
<td>0.24</td>
</tr>
<tr>
<td>Proportion of ART restorations of total number of restorations placed</td>
<td>72%</td>
<td>27%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of treatments</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ex extractions</td>
<td>1941</td>
<td>891</td>
</tr>
<tr>
<td>Non-ART restorations</td>
<td>190</td>
<td>313</td>
</tr>
<tr>
<td>ART restorations</td>
<td>29</td>
<td>59</td>
</tr>
<tr>
<td>Restoration - Extraction ratio (REX)</td>
<td>0.18</td>
<td>0.39</td>
</tr>
<tr>
<td>Proportion of ART restorations of total number of restorations placed</td>
<td>20%</td>
<td>22%</td>
</tr>
</tbody>
</table>
therefore, patient load/work load and clinical ART skill were the two barriers that had the most and the least influence, respectively on the implementation of ART in the public oral health care system studied.

The barrier factors under study appeared to have less influence in inhibiting the utilisation of ART in primary dentitions of children than of adults. It has been shown that children accept the ART procedures better than they accept traditional restorative procedures\textsuperscript{21,25} and, furthermore, they respond more fearfully to invasive procedures, such as injections and high speed drilling, than most adults do. As patient anxiety is directly related to operator stress\textsuperscript{3,11,17,31}, operators may have tried to reduce stress by using the ART approach, which may explain the higher use of ART in treating children than in adults.

However, that issue was not relevant for all dentists under study, as it was also shown that operators’ clinical skills in mastering the ART procedures were the only factor that influenced the utilisation of ART in children. Dentists who perceived their levels of ART skills to be low produced fewer ART restorations in primary teeth than colleagues more confident in applying ART. The three days allocated to the ART training may have been insufficient for a number of dentists and dental therapists to master the clinical skills necessary for performing ART in children with sufficient confidence: particularly, those apprehensive about treating children through traditional restorative procedures. Those desiring to improve their skills in treating them would probably have benefited from a follow-up meeting after some months or from extension of the initial training course by a couple of days geared towards providing more practical training.

Adult patients’ generally less fearful response to invasive traditional dental treatment may have reduced the need for operators to resort to the use of ART in treating them. Lower utilisation of ART for permanent teeth in adult patients than in children may also be due to the operators perception that ART is more appropriate for use in primary than in permanent teeth.

Material supply was the only factor that inhibited the provision of both ART and traditional restorative care in both dentitions, relative to tooth extraction. A low availability, or even absence, of materials/instruments needed to perform restorations, resulted in dentists’ performing more extractions than restorations. It is obvious that the lack of a sufficient restorative material and instruments/equipment supply to clinics prohibited operators from implementing restorative care.

The strongest barrier factor affecting implementation of

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|}
\hline
\textbf{Primary dentition} & \textbf{Barrier factors} & \textbf{Mean REX score} & \textbf{ART \% of the total number of restorations placed} \\
\hline
\hline
TOTAL & 0.15 & -0.58* \\
Patient load & 0.17 & -0.31 \\
Operator opinion & 0.35 & -0.40 \\
Patient opinion & -0.06 & -0.34 \\
Service management & -0.06 & -0.33 \\
Material supply & 0.48* & -0.40 \\
Clinical ART skills & 0.19 & -0.63** \\
Chair side assistance & -0.29 & -0.15 \\
\hline
\textbf{Permanent dentition} & \textbf{Barrier factors} & \textbf{Mean REX score} & \textbf{ART \% of the total number of restorations placed} \\
\hline
TOTAL & 0.35 & -0.84** \\
Patient load & 0.39 & -0.54* \\
Operator opinion & 0.39 & -0.53* \\
Patient opinion & 0.13 & -0.76** \\
Service management & -0.04 & -0.46* \\
Material supply & 0.49* & -0.29 \\
Clinical ART skills & 0.30 & -0.44 \\
Chair side assistance & -0.03 & -0.57* \\
\hline
\end{tabular}
\caption{Correlations between barrier factors and mean REX scores and the proportion of ART restorations in the total number of restorations placed per dentition}
\end{table}

*p-value: Pearson correlation test: *0.01<p<0.05, **p< 0.01
the ART approach in the health services was the high patient load/work load. Other barrier factors that significantly hindered the use of ART in permanent teeth were operator opinion, patient opinion, oral health service management and chair-side assistance. Not surprisingly, having to treat a high number of patients daily creates treatment-time pressure on operators and results in long waiting times for patients. Under such circumstances it is difficult to introduce new treatment methods such as the ART approach uses. If at the same time services are insufficiently managed and chair-side assistance is inadequately available, operators are hardly likely to see introducing a change as beneficial. This means that if the health authorities would like to improve the oral health services through increasing the number of restorations and reducing the number of extractions, they have to employ more dentists and supporting staff and ensure availability of sufficient materials, instruments and functional dental equipment, in addition to providing support through guidance and leadership. Without specific guidelines and targets, and a monitoring system managed by health authorities, operators tend to ignore the necessity to introduce new methods in their daily practice and may do little to inform patients about their benefits.

A general resistance by operators towards adopting changes into their daily dental practices may also have particular importance in causing negative operator opinion of ART. Such resistance may not be specific to ART but related to psychosocial factors which influence the spread of innovations. Innovations, such as the ART approach, may be perceived either as improvements or as disruption. Either perception depends upon the existence of obvious disadvantages of traditional methods in comparison to innovation. If any such disadvantages are absent, an innovation may often be rejected despite its advantages in other fields. Furthermore, the reasons for adoption or rejection may also depend on interpersonal communications between operators about their clinical experiences, and on the influence of opinion leaders and experts. Disagreements between experts may lead to operator insecurities about innovations and thus also hinder their adoption.

In view of the above, possible barriers should in future be identified before introducing the ART approach into a public oral health service system. The types and effects of barrier factors may differ from situation to situation. Such information would prove useful to those deciding whether barrier factors can be addressed and whether the implementation of the ART approach after training is likely to succeed or fail. Van Palenstein-Helderman, et al. (2003) confirmed that experience in implementing ART in the oral health care system, particularly in relation to its effectiveness, efficiency and sustainability under local conditions, is lacking. In addition to an initial situation analysis, small-scale demonstration projects could help in revealing potential barriers. In order to address general resistance to change, interactive hands-on training followed by continued refresher courses and encouragement of interpersonal communications should be encouraged as these measures have been shown to be effective.

**CONCLUSIONS**

It was concluded that the strongest barrier to introducing ART was a high patient load. Insufficient supply of dental materials and instruments, and dentists’ perceptions of low levels of clinical skills in performing ART confidently after training were the two major barriers to utilising ART in children. Inadequate materials/instruments provision, negative operator and patient opinion, and poor management of services by health authorities were factors that inhibited the proper utilisation of ART among adults in the public oral health service of the Ekurhuleni region 12-months post-ART training.

<table>
<thead>
<tr>
<th>Barrier factor</th>
<th>Patient load</th>
<th>Operator opinion</th>
<th>Patient opinion</th>
<th>Service management</th>
<th>Material supply</th>
<th>Clinical ART skills</th>
<th>Chair side assist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient load</td>
<td>0.1%</td>
<td>0.1%</td>
<td>29.3%</td>
<td>9.9%</td>
<td>11.1%</td>
<td>50.2%</td>
<td></td>
</tr>
<tr>
<td>Operator opinion</td>
<td>0.70*</td>
<td>0.0%</td>
<td>2.6%</td>
<td>33.1%</td>
<td>6.9%</td>
<td>66.3%</td>
<td></td>
</tr>
<tr>
<td>Patient opinion</td>
<td>0.73**</td>
<td>0.77**</td>
<td>1.1%</td>
<td>46.4%</td>
<td>9.4%</td>
<td>7.5%</td>
<td></td>
</tr>
<tr>
<td>Service management</td>
<td>0.26</td>
<td>0.52*</td>
<td>0.57**</td>
<td>51.8%</td>
<td>37.1%</td>
<td>16.1%</td>
<td></td>
</tr>
<tr>
<td>Material supply</td>
<td>0.40</td>
<td>0.24</td>
<td>0.18</td>
<td>-0.16</td>
<td>11.3%</td>
<td>43.5%</td>
<td></td>
</tr>
<tr>
<td>Clinical ART skills</td>
<td>0.39</td>
<td>0.44</td>
<td>0.40</td>
<td>0.22</td>
<td>0.38</td>
<td>91.3%</td>
<td></td>
</tr>
<tr>
<td>Chair side assistance</td>
<td>0.17</td>
<td>0.11</td>
<td>0.42</td>
<td>0.43</td>
<td>-0.19</td>
<td>-0.03</td>
<td></td>
</tr>
</tbody>
</table>

Correlation coefficients
p-value: Pearson correlation test: *0.01<p<0.05, **p<0.01
ACKNOWLEDGMENTS

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