Abstract: Chemotherapy and radiotherapy are aggressive treatments for cancer management. Both therapies make the stomatogastic system vulnerable to adverse effects on the oral mucosa and hard tissues. This may result in severe oral complications that can affect the quality of life of the oncologic patient. Consequently, oral diagnosis and interdisciplinary management by the stomatologist are critical for cancer treatment, regardless of its location. Objective. To determine the oral health status of cancer patients before, during and after antineoplastic treatment at a cancer institute in the city of Barranquilla, Colombia. Materials and Methods. A descriptive, longitudinal and prospective study of 131 cancer patients, was conducted. The study consisted of initial stomatological assessment of the antineoplastic therapy; classification according to the antineoplastic therapy given by the oncologist; a second stomatological assessment during treatment; and a final stomatological assessment or evaluation forty days after the end of therapy. Descriptive statistics, chi-square and MacNemar test were used to compare and identify variances at the different stages. Results. Female patients accounted for 69%, and breast cancer had 24% prevalence among the included subjects. At the initial stomatological assessment, high frequency lesions were identified, such as generalized biofilm-associated gingivitis in 69% of the cases, followed by oral candidiasis in 61%. The specific prevalence of lesions was 10.65%. In the second stomatological assessment, a greater frequency of periodontal abscesses was observed in 31%, and oral mucositis type II in 18%. The third clinical assessment showed significant changes in oral health status; an increase in the frequency of gingivitis was found in 9.9% ($p<0.001$); unlike before and during, there was an increment in dental caries of 26.73% ($p<0.00000$) at this last stage, root remains increased by 39.53% ($p<0.00000$), and finally, xerostomia increased by 45%. Oral candidiasis was the only lesion that showed improvement. Conclusion. An increase in the number of lesions was observed during and after antineoplastic treatment. The oral cavity is susceptible to antineoplastic treatments; gingivitis, candidiasis, xerostomia, and mucositis were observed, among others conditions. Keywords: Neoplasms; medical oncology; oral health; diagnosis, oral radiotherapy; antineoplastic agents.
INTRODUCTION.

Cancer may affect any tissue or organ, and it can be associated with socio-demographic, genetic and congenital factors, and alcohol or tobacco consumption, all of which may contribute to its development. Once the diagnosis and the degree of tumor extension have been established by the oncologist, decisions are made about the most appropriate and effective treatment that may prolong patient survival.

One or several treatment modalities are carefully selected and may include cancer surgery, radiotherapy or chemotherapy. These antineoplastic treatments disrupt the proliferation of rapidly multiplying cells by different mechanisms of antitumor action, by decreasing the size of the cancer. The latter has direct effects on other organs and tissues that heal rapidly.

Since normal cells in the lining of the mouth also multiply quickly, cancer treatment prevents their proliferation, which makes normal repair of oral tissues difficult, resulting in oral lesions characteristic of oncological treatment. Chemotherapy and radiotherapy are aggressive treat-ments for cancer management. Both therapies make the stomatogatic system vulnerable to adverse effects on the oral mucosa, hard tissues, and other surrounding tissues.

Side effects result in aggressive oral complications such as Oral Mucositis (OM) at its different stages, acute gingivitis, osteoradionecrosis, xerostomia, trismus, increased caries and oral candidiasis, among other infectious lesions. These conditions may appear due to immunosuppression caused by antineoplastic treatments or may have been preexisting in the oral cavity and become aggravated due to the oral cavity’s low biological response, which hinders the recovery of the mucosa following the effect of irradiation, chemical agents and microorganisms. Head and neck cancer studies report that the closer the cancer is to the oral cavity, the more negative its effects are.

Patients diagnosed with cancer are affected by psychological distress and usually neglect their oral health care, which in turn undermines their general health status. In this context, the oral health provider must generally implement a stomatological protocol which consists of removing septic foci to prevent complications after and during oncotherapy and reduce the microbiological load. Additionally, this would provide optimal conditions for healthy nutrition and a better quality of life.

To prevent these complications, the dentist must play a key role in the multidisciplinary oncology team and in the prevention and defense stages, participating in the diagnosis of cancer, during and after or at the end of treatments.

The latest report of the Colombian National Cancer Institute (INC, for its acronym in Spanish), part of the national plan for cancer control in Colombia 2012-2020, highlights objectives such as the search based on guidelines to reduce preventable cancer mortality and improve the quality of life of cancer patients. These guidelines include the palliative management of complications, and the treatment and care of the oral cavity in cancer patients.
Regardless of the anatomical location of the tumor) by the nursing staff, and not specifically by a stomatologist.\textsuperscript{14}

There is little bibliographic support at local and regional level showing the interaction of oral health professionals in the management, evolution, prevention and treatment of complications before, during and after cancer treatment. There is no evidence that such inter-action has been mandatory or encouraged by government health agencies.\textsuperscript{15,16-20} The aim of this study is to determine the oral health status of cancer patients before, during and after antineoplastic treatment at a cancer institute in the city of Barranquilla, Colombia.

**MATERIALS AND METHODS.**

A longitudinal, prospective and descriptive study was conducted involving a population of 420 patients, non-probabilistic sampling at convenience, eventually consisting of 131 cancer patients from an oncological institute in the city of Barranquilla, Colombia.

Selection criteria included: patients over 18 years of age with a diagnosis of cancer in any anatomical location; patients who had not started antineoplastic treatment; patients who had not been under dental treatment 40 days before the oncological diagnosis, and in optimal cognitive status.

The national ethical considerations in force according to the resolution 008430 of 1993 were taken into account, under the agreements of the world medical association for human research and the Helsinki Agreement. Before being asked to sign the inform consent, participants were informed of the research objectives and benefits.

The study was divided into three stages:

Stage one consisted of an intra- and inter-examiner calibration to obtain a Kappa analysis higher than 0.80. The examiners with better conditions to perform the stomatological diagnoses were compared with an expert stomatologist who had over 8 years of experience.

Calibration was obtained through the oral clinical evaluation of 30 patients in similar conditions. After this process, patients under study, prior to the oncological diagnosis confirmed by the oncologist, underwent an intra-extra oral stomatological examination to identify pre-existing pathologies.

Data were registered in an instrument that on this occasion was called medical history, which included the following data: full name, age, occupation, residential address, and identification number.

It also included aspects such as the reason for oncological consultation, oncological diagnosis, family, psychosocial and personal history, habits and vices, previous evaluations of organs and systems, extra-oral and intra-oral physical examination, radiographic evaluation (panoramic), all this in order to perform impressions and diagnoses, and to develop a comprehensive stomatological preventive plan.

In the second stage of the study, before the start of chemotherapy, radiotherapy and oncologic surgical interventions, the application of a preventive management protocol was performed.

The protocol included:

Promotion and prevention of stomatological lesions associated with treatments for cancer, teaching of oral hygiene habits, management and hygiene of prostheses, conditioning of the oral cavity to receive chemo-radiotherapy, donation of oral hygiene elements, among others. Stomatological lesions were managed by stomatologists and/or referred to different specialties of their healthcare provider (EPS, for its acronym in Spanish).

After the application of these guidelines, the antineoplastic therapies began: chemotherapy, radiotherapy and cancer surgery. The patients under study were grouped as follows (for the purposes of this research and according to the oncologist’s criteria):

- **Group 1:** chemotherapy + cancer surgery + radiotherapy.
- **Group 2:** radiotherapy + chemotherapy.
- **Group 3:** chemotherapy + cancer surgery (or vice versa)
- **Group 4:** cancer surgery + radiotherapy (or vice versa)
- **Group 5:** radiotherapy only
- **Group 6:** chemotherapy only
- **Group 7:** cancer surgery only.

During the antineoplastic therapy process, the research group continued with the programs for the promotion and prevention of oral complications and involvement of structures connected with the stomatognathic system. Then a second stomatological examination was performed to monitor the evolution of the oral health status of these patients.
Finally, 40 days after the completion of the last antineoplastic session, a final stomatological clinical examination was performed at the third stage for the evaluation of the oral health status after the completion of the antineoplastic treatments.

A descriptive analysis was performed for the nominal and ordinal variables, obtaining prevalence, percentage, average, proportion, mean, Standard Deviation (SD), and analysis of variance. Likewise a chi-square and MacNemar test were performed to compare the behavior of the variables, before, during and after. Results were evaluated according to a $p$-value equal to or greater than 0.05 for statistical significance.

**RESULTS.**

Females and males accounted for 69% and 31% of the patients under study ($n=131$), respectively; 47% ranged between 41 and 60 years old (SD: 14.77 years, and an average of 60.7 years of age); 55% came from locations outside the city of Barranquilla, Colombia, however, the majority came from municipalities and rural areas of the department of Atlántico, and others such as Sucre and La Guajira, Colombia. (Table 1)

As for the types of cancer, breast cancer had a frequency of 24%, followed by thyroid cancer (11%) and prostate cancer. The presence of different types of tumors in diverse anatomical locations was observed, such as: cervix, colon, ovary, and lung. (Table 2)

It is interesting to highlight that 55% of the cervical, thyroid, ovarian, stomach and breast tumors corresponded exclusively to female patients, exceeding 50% of the patients studied in the present research.

About half (51.14%) of the sample under study was treated exclusively with chemotherapy, followed by chemotherapy combined with radiotherapy (12.21%). Other treatments for cancer control were also identified, such as cancer surgery, and the combination of several antineoplastic therapies. (Table 3)

**Stomatological lesions found before starting antineoplastic therapies**

In the first assessment, stomatological lesions were identified in all patients. No patient had a 100% healthy oral cavity; an average of 10 lesions per patient was observed. Patients reported not having been referred to the general dentistry/stomatology service at any point after diagnosis. In this first assessment, the frequency of lesions was led by generalized biofilm-associated gingivitis observed in 69% of the cases, followed by oral candidiasis in 61%, as well as other conditions in varying frequencies. (Table 4)

Additionally, absence of secondary lesions typically caused by antineoplastic treatments was observed, which were found later during the second and third assessments. The specific prevalence of lesions in this stage of the study was 10.65% of the total population of individuals susceptible to cancer in the city of Barranquilla, Colombia.

**Stomatological lesions found during antineoplastic therapies**

The second stomatological assessment was performed half-way through the application of antineoplastic therapies. The lesions found most frequently in the first stage increased their incidence, (some remained invariable, some have significantly increased and others not previously identified were now observed). Generalized biofilm-associated gingivitis increased to 74%; 6.59% over the value obtained in the first assessment. On the other hand, oral candidiasis decreased its incidence by 56%, 6.85% lower than in the first clinical assessment.(Table 4)

Subjective lesions such as xerostomia increased from 25% to 61%. Trismus, absent in the first assessment, accounted for 30% in the second one. Other infectious processes such as periodontal abscesses that in the first clinical assessment had a low frequency increased their incidence 14 points in this second assessment by 31% (63%). Oral mucositis type II and type III, absent in the first assessment, showed a frequency of 18% in the second one, a difference of 13.04%.

Other lesions that were absent in the first stomatological evaluation were observed in the second clinical assessment, such as: osteoradionecrosis, radiation caries, stomatodynia, atrophic tongue, xerostomia, geographic tongue and hyperplasia. (Table 4).

Stomatological lesions found after antineoplastic therapies and their relationship with previous assessments Forty days after completing the antineoplastic therapies, a third clinical assessment was carried out. The third assessment identified significant changes in the oral health
status of the cancer patients under study. There was a statistically significant increase in the frequency of lesions such as: generalized biofilm-associated gingivitis, with a difference of 9.9%, and 95% confidence interval (CI), \(p\)-value<0.001; dental caries, which increased by 26.73% with respect to the first assessment, \(p<0.00\).

Similarly, an increase in the frequency of appearance of saburral tongue was found in 29.9%, unlike the first assessment with \(p<0.00\). Root remains also increased by 39.53% in contrast to the first stomatological assessment \(p<0.00\); and finally xerostomia increased its incidence by 45%, in contrast with the first assessment, with a \(p\)-value<0.05. Other conditions increased with respect to their frequencies of appearance at the first and second clinical assessments, such as: dental attrition, dental abrasion, actinic cheilitis, trismus, temporo-mandibular joint disorders (TMJ), and sub-prosthetic stomatitis in its three types of occurrence. (Table 4)

Lesions that remained without significant changes due to their clinical nature and despite the use of

### Table 1. Frequency and percentage according to sociodemographic characteristics of the sample under study.

| Variable       | Frequency (N=131) | %  |
|----------------|-------------------|----|
| Sex            |                   |    |
| Female         | 90                | 69 |
| Male           | 41                | 31 |
| Age (Range)    |                   |    |
| 26 – 40        | 12                | 9.0|
| 41 – 60        | 62                | 47 |
| >61            | 57                | 44 |
| Place of origin|                   |    |
| Barranquilla   | 59                | 45 |
| Outside Barranquilla | 72 | 55 |

### Table 2. Frequency and percentage according to oncologic disease.

| Oncologic diagnosis (Type of Cancer) | Frequency (N=131) | %  |
|--------------------------------------|-------------------|----|
| Breast                               | 32                | 24 |
| Prostate                             | 15                | 11 |
| Thyroid                              | 14                | 11 |
| Stomach                              | 6                 | 6  |
| Liver                                | 2                 | 1  |
| Lung                                 | 8                 | 6  |
| Esophagus                            | 6                 | 5  |
| Colon                                | 11                | 8  |
| Cervix                               | 10                | 8  |
| Ovary                                | 9                 | 7  |
| Skin                                 | 2                 | 2  |
| Brain                                | 2                 | 2  |
| Leukemia                             | 11                | 8  |
| Lymphoma                             | 3                 | 2  |

### Table 3. Frequency and percentage according to the type of antineoplastic therapy.

| Type of Antineoplastic Therapy       | Frequency (N=131) | %  |
|--------------------------------------|-------------------|----|
| Chemotherapy, surgery and radiotherapy| 11                | 8.39|
| Radiotherapy and Chemotherapy        | 16                | 12.21|
| Chemotherapy and surgery             | 18                | 13.74|
| Surgery and radiotherapy             | 16                | 12.21|
| Radiotherapy                         | 9                 | 6.87 |
| Chemotherapy                         | 67                | 51.14|
| Oncologic surgery                    | 8                 | 6.10 |
| Other                                | 2                 | 1.52 |
Table 4. Comparison of stomatological lesions; before, during and after antineoplastic therapies of the sample under study (N=131).

| Lesion                                      | Before N | %   | During N | %   | After N | %   | % of changes Before/ during | Changes | % of changes During/ after | X² of MACnemar | p-value |
|---------------------------------------------|----------|-----|----------|-----|---------|-----|-----------------------------|---------|---------------------------|----------------|---------|
| Simple generalized biofilm-associated gingivitis | 91  69   | 97  74 | 101  77  | 6.59 | *↑4.12  | ↑9.90 | 12.1 | <0.001
| Simple localized biofilm-associated gingivitis | 40 31    | 40 31 | 55 42    | 0.00 | 37.50   | ↑27.27 | 25.6 | <0.001
| Chronic periodontitis                       | 60 46    | 61 47 | 70 53    | 1.67 | ↑14.75  | +/- 14.29 | 12.1 | <0.001
| Frictional hyperkeratosis                   | 14 11    | 21 16 | 21 16    | 50.0 | 0.00    | ↑33.33 | 6.4  | >0.01
| Xerostomia                                  | 33 25    | 80 61 | 60 46    | 14.42 | ↑25.00  | ↑45.00 | 78.4 | <0.05
| Saburral tongue                             | 68 52    | 79 60 | 97 74    | 16.18 | ↑22.78  | ↑29.90 | 90   | <0.00000
| Oral candidiasis                            | 80 61    | 73 56 | 78 60    | 8.75  | **↓6.85 | ↓2.56 | 0.1  | >0.01
| Type I Sub-Prosthetic Stomatitis            | 35 27    | 33 25 | 35 27    | 5.71  | ↓6.06   | 0.00  | 0.1  | >0.01
| Type II Sub-Prosthetic Stomatitis           | 9 7      | 24 18 | 28 21    | 166.67 | ↑16.67  | ↑67.86 | 40   | <0.05
| Type III Sub-Prosthetic Stomatitis          | 4 3      | 11 8  | 15 11    | 175.00 | ↑36.36  | ↑73.33 | 14.4 | <0.05
| Leukoedema                                  | 6 5      | 32 24 | 35 27    | 433.33 | ↑9.38   | ↑82.86 | 90   | <0.00000
| Actinic cheilitis                           | 8 6      | 33 25 | 37 28    | 312.50 | ↑12.12  | ↑78.38 | 90   | <0.00000
| Partial edentulism                          | 55 42    | 65 50 | 75 57    | 18.18  | ↑15.38  | ↑26.67 | 44.1 | <0.05
| Total edentulism                            | 39 30    | 43 33 | 50 38    | 10.26  | ↑16.28  | ↑22.00 | 14.4 | <0.05
| Attrition                                   | 59 45    | 60 46 | 73 56    | 1.69   | ↑21.67  | ↑19.18 | 22.5 | <0.05
| Abrasion                                    | 27 21    | 27 21 | 35 27    | 0.00   | ***+/- 29.63 | ↑22.86 | 8.1  | <0.05
| Caries                                      | 74 56    | 98 75 | 101 77   | 32.43  | ↑3.06   | ↑26.73 | 78.4 | <0.00000
| Root remains                                | 52 40    | 70 53 | 86 66    | 34.62  | ↑22.86  | ↑39.53 | 122.5 | <0.00000
| Periodontal abscesses                       | 19 15    | 41 31 | 47 36    | 11.79  | ↑14.63  | ↑59.57 | 84.1 | <0.00000
| Chronic pulpitis                            | 36 27    | 39 30 | 41 31    | 8.33   | ↑5.13   | ↑12.20 | 3.6  | >0.01
| Tumors                                      | 0 0      | 3 2   | 5 4      | 2.00   | ↑66.67  | ≤100.00 | 3.6  | <0.05
| Cysts                                       | 0 0      | 2 2   | 2 2      | 2.00   | 0.00    | ↑100.00 | 0.9  | <0.05
| Petechiae                                   | 3 2      | 25 19 | 27 21    | 7.33   | ↑8.00   | ↑88.89 | 62.5 | <0.05
| Ecchymosis                                  | 10 8     | 15 11 | 33 25    | 5.00   | ↑12.00  | ↑69.70 | 57.6 | <0.05
| Trismus                                     | 0 0      | 30 23 | 43 33    | 30.00  | ↑43.33  | ↑100.00 | 193.6 | <0.05
| Temporomandibular joint disorders.          | 8 6      | 9 7   | 13 10    | 12.50  | ↑44.44  | ↑38.46 | 3.6  | >0.01
| Palatine torus                              | 28 21    | 28 21 | 28 21    | 0.00   | +/- 0.00 | +/- 0.00 | 0.1  | >0.01
| Mandibular torus                            | 55 42    | 55 42 | 55 42    | 0.00   | +/- 0.00 | +/- 0.00 | 0.1  | >0.01
| Type II mucositis                           | 0 0      | 23 18 | 20 15    | 23.00  | ↑13.04  | ↑100.00 | 44.1 | <0.00000
| Type III mucositis                          | 0 0      | 18 14 | 22 17    | 18.00  | ↑22.22  | ↑100.00 | 52.9 | <0.00000
| Osteoradionecrosis                          | 0 0      | 13 10 | 10 8     | 13.00  | ↑23.08  | ↑100.00 | 12.1 | <0.00000
| Radiation caries                            | 0 0      | 1 1   | 1 1      | 1.00   | 0.00    | ↑100.00 | 0.4  | >0.00000
| Stomatodynia                                | 0 0      | 8 6   | 12 9     | 8.00   | ↑50.00  | ↑100.00 | 16.9 | >0.00000
| Atrophic tongue                             | 0 0      | 11 8  | 11 8     | 11.00  | 0.00    | ↑100.00 | 14.4 | >0.00000
| Hyposialia                                  | 0 0      | 1 1   | 1 1      | 1.00   | 0.00    | ↑100.00 | 0.4  | >0.00000
| Geographic tongue                           | 0 0      | 1 1   | 1 1      | 1.00   | 0.00    | ↑100.00 | 0.4  | >0.00000
| Hyperplasias                                | 0 0      | 8 6   | 11 8     | 8.00   | ↑37.50  | ↑100.00 | 14.4 | >0.01

*↑: Increased. **↓: Decreased. ***+/-: Remained invariable. N: cancer patients.
stomatological palliative therapies and controls included localized biofilm-associated gingivitis, chronic periodontitis, tumors (for example: palatine and mandibular torus), and cysts (residual and periapical).

The only lesion that showed signs of improvement in the last assessment compared with the initial one was oral candidiasis, improving by 2.56% with a statistically significant $p$-value of $<0.05$. (Table 4)

**DISCUSSION.**

Cancer in Colombia is an increasing public health problem. It has major psycho-affective, social and economic repercussions, posing a challenge for the health system as a whole, including oral health care. In this context, the role played by the dentist is essential since the early management of the cancer patient is critical, even in those patients without oral lesions and presence of risk factors; since the detection of the cancer only becomes possible when the patient describes symptoms or when the condition becomes noticeable or at advanced stages.

In this study, the greatest number of cancer cases was observed in patients aged between 40 and 60 years, affecting mainly females 69%. This is related to the fact that breast cancer is the most frequent type of cancer, accounting for 24%.

The study allowed for the identification of some variables such place of origin (most affected patients came from outside Barranquilla, from municipalities of the Atlantico department), although there was not a significant difference in the number of patients affected with cancer who lived in the city at the time of the study, according to epidemiological data reported by the INC. 14

Approximately 14 million new cases of cancer diagnosed worldwide were estimated in 2012; of these 71,442 cases corresponded to Colombia. According to Globocan projections for 2015, 79,660 people with cancer are expected in Colombia, with a higher incidence in women under 65 and by 2035, about twice as many cases are expected to be reported (152,901) mainly in men over 65 years of age. 15 Álvarez et al., 8 show in their study that of a sample of 100 patients with breast cancer, 95.1% (n=77) presented periodontal disease, and in 39.5% mucositis was the trigger that aggravated their condition after antineoplastic treatment. 26-28

In this study, oral manifestations consistent with antineoplastic treatment included generalized gingivitis, oral candidiasis, xerostomia and trismus, which were all initially absent. All cancers lead to complications that can deteriorate the patient’s quality of life, these can occur before, during or after antineoplastic treatment.

Regarding the oral manifestations observed during and after treatment, a study conducted in Madrid, Spain, by Sabater et al., 27 showed that the main oral complications of chemo-radiotherapy were: mucositis, xerostomia, gingival infections and bleeding. Mucositis was the most frequent, with a prevalence ranging between 30-85%, and one of the major causes of morbidity after the administration of antineoplastic treatment.

This secondary complication alters important functions such as phonation, feeding and swallowing, and is accompanied by pain. 29 These data were compared with this study demonstrating that mucositis is one of the most common conditions in cancer patients undergoing cancer treatment; changing from 0% at the first stage to 18% during the treatment, and 15% after the antineoplastic therapy ends.

With respect to other oral conditions it was found that oral candidiasis, xerostomia and subprotic stomatitis type I had a positive change during the treatment. Combined radiotherapy and chemotherapy caused more oral infections compared to palliative care and surgery. 28 Other studies conducted by authors such as Jacobo et al., 30 and Rocha et al., 19 suggest that the most frequent oral conditions in patients undergoing antineoplastic treatments were xerostomia, trismus and mucositis.

However, all the abovementioned studies mainly focus on the wide variety of side effects presented during and after antineoplastic treatment, showing a similar prevalence of some of the oral manifestations when compared with this study. Still, none of them describe oral manifestations observed before the start of the treatment (as the ones included in the present study), so it must be assumed that only a very small number of studies assess the oral health status of patients before or at the beginning of antineoplastic therapies.
The reviewed literature shows that there is little evidence of studies where cancer patients who will soon receive therapy are assessed and treated by a stomatologist. Even more, this previous oral assessment by a stomatologist and a multidisciplinary team is not included in any of the protocols established in the Colombian legal statutes for the treatment of this type of patients.1,14,26

CONCLUSION.

The present study shows a recurrent relationship between conditions in the oral cavity and antineoplastic treatments in patients with cancer before, during and after treatment, showing a greater prevalence of side effects such as generalized biofilm-associated gingivitis, candidiasis, xerostomia, mucositis.

At the different stomatological assessments and evaluations carried out during the antineoplastic treatment it was possible to verify in the initial stage that no patient was fully healthy. Consequently, it is possible to conclude that no one had an optimal oral health status. In the second stage, there was an increase of some secondary lesions in relation to the treatment received and, in turn, new oral conditions appeared.

At the last treatment stage, a certain period of time is needed for cell turnover and healing, however, from a clinical and statistical point of view, a significant increase in oral lesions was observed as a result of antineoplastic treatments. It should be noted that oral candidiasis was the only lesion that showed significant improvement at the time of the last assessment.

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