# Introduction

**Juvenile idiopathic *arthritis* (JIA)** often causes significant functional ~~impairment~~ throughout the lifespan [1,2]. Medical workers who are aware of the JIA’s clinical course specifics in adolescence can provide better assistance at the transition stage when a patient’s healthcare shifts from a pediatric to an adult health services [3, 4,5]. The patient's transmission is a multidimensional, interdisciplinary and active process, which addresses the medical, socio-psychological and educational/professional needs of adolescents with JIA [6,7,8]. Previous studies have shown that the use of specific questionnaires (CHQ, Peds-QL) don’t allow fully assess psychometric changes in young adults. In particular, the interpretation of these studies’ results on Peds-QL is limited due to a small sample size [10]. On the contrary, when using HR-QOL, Haverman L. et al. (2011) found significant changes in the quality of life in children and adolescents with JIA [11].

## Heading 2

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The HAQ (Moroz & Bezsheiko, 2018) questionnaire is widely used in clinical practice for the study rheumatic diseases in adults, particularly in rheumatoid arthritis [12]. This questionnaire is a useful tool for evaluation of functional status, its change during treatment (Frankova & Semenoga, 2014). HAQ score is also associated with disease activity, mortality, and need in joint replacement [12, 13]. Most often, for the quality of life (QoL) assessment in adult patients, the SF-36 questionnaire is used [13]. Indeed, QoL in adulthood may be influenced by sociological, economic, philosophical and ethical factors, which can be less informative in childhood. For patients in the transitional period from pediatric to adult medical care, it is necessary to investigate the effectiveness of various medical examination methods for measuring QoL.

**The study aimed** to determine the impact of the disease on the QoL in young adults with JIA during the transition from a pediatric to an adult healthcare service.

# Materials and methods

## materials

A study sample included 89 young people aged 16 to 22 years old with a history of JIA, regardless (1) of the active inflammation severity at the time of examination and 25 healthy young volunteers that formed the control group. The experimental group comprised of patients from different Ukrainian who were diagnosed with the JIA according to the classification criteria of the International League of Associations for Rheumatology - ILAR [14] between 1984 and 2014 without severe concomitant pathology. Upon reaching adulthood, all patients with JIA were examined by an adult rheumatologist during outpatient visits or inpatient at the Oleksandrivka City Clinical Hospital in Kyiv between April 2015 and February 2017. In the study were analyzed demographic and clinical data, including age, gender, delayed diagnosis of JIA, disease duration, number of swollen joints, limitation of joint mobility, disease activity, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Pain and overall well-being were measured using the visual analogue scale (VAS). The functional status was evaluated using the HAQ questionnaire (Health Survey). Disease activity and the presence of remission were determined according to the American Association of Rheumatologists criteria [15].

## methods

### First Method

Additionally, the data regarding current JIA treatment were analyzed, including the use of non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids (GCs), methotrexate, leflunomide, hydroxychloroquine, azathioprine and biological therapy (IL-1Ra, anti-TNF agents (etanercept, adalimumab), abatacept and tocilizumab).

The QoL of patients with JIA and the control group was assessed using the Short-Form-36 questionnaire (SF-36). We used licensed access containing (license No. QM037587) for Non-Profit Academic Research from the Management of Scientific Grants and Research (OGSR) provided by OptumInsight Life Sciences, Inc..

### Second Method

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# Statistical analysis

Statistical analysis was performed using descriptive statistics, Student's criteria for unbound variables, and one-way ANOVA dispersion analysis. The data are presented as the mean ± standard deviation (SD) for continuous variables and numbers (percentages) for categorical variables. Statistically significant was the probability value p <0,05. The correlation was determined by the Pearson method for a two-way mixed model. In the analysis, software packages "Statistica 6.0" was used by Copyright StatSoft, Inc. 1984-2001.

# Results

There was conducted an analysis of demographic and anthropometric data from 89 young patients with JIA and 25 healthy volunteers (Table 1). The mean age of patients was 19.4 ± 1.8 years, which did not significantly differ from the mean age in control group. The average duration of the disease was 8.7 ± 5.1 years and the average age of the disease onset - 10.2 ± 4.9 years. The mean time from the disease’s onset to the diagnosis was estimeated at 15.6 ± 25.9 months.

The oligoarthritis form of JIA was diagnosed in 34 patients, including 20 patients with persistent and 14 with common form. The polyarthritis variant was found in 24 patients, from whom 10 had seropositive and 14 had seronegative polyarthritis. Enthesitis-related arthritis and psoriatic arthritis were diagnosed in 18 patients, and systemic JIA - in 13 patients.

Most patients (67.4%) had previously received glucocorticoids (GCs) before baseline period, and at the time of observation, only 27% received GCs. 14 patients received only NSAIDs. 75 patients received DMARD, including methotrexate (n=55), plaquenil (n=12), sulfasalazine (n=6), azathioprine (n=2). 23 patients received immunobiological therapy before or at the time of examination; 19 patients were prescribed monoclonal antibodies to the TNF-19 (etanercept - 16 patients, adalimumab - 3 patients), 2 - tocylumizabac, and remaining 2 - rituximab. Remission was diagnosed in 37 (41.6%) patients with a history of JIA.

Table 1. Demographic characteristics of patients with JIA.

|  |  |
| --- | --- |
|  | Patients with JIA (n=89) |
| Sex (M/F) | 41/48 (control group -12/13 |
| Middle age | 19.4±1.8 (control group - 20.1±1.9) |
| Duration of the disease, years | 8.7±5.1 |
| Age at onset of JIA, years | 10.2±4.9 |
| Time from onset to the diagnosis, months. | 15.6±25.9 |
| Persistent oligoarthritis | 20 (22.5%) |
| Common oligoarthritis | 14 (15.7%) |
| Polyarthritis RF + | 10 (11.2%) |
| Polyarthritis RF - | 14 (15.7%) |
| Enthesitis-related arthritis + psoriatic arthritis | 18 (16.9%) |
| Systemic JIA | 13 (14.6%) |
| GCs took earlier / at the moment | 60 (67.4%)/24 (27%) |
| Remission | 37 (41.6%) |
| NSAIDs | 14 |
| DMARD (n=75) | |
| Methotrexate | 55/75 |
| Plaquenil | 12/75 |
| Sulfasalazine | 6/75 |
| Azathioprine | 2/75 |
| Immunobiology (n=23) | |
| Anti-TNF (ETA / ADA)) | 19/23 (16/3) |
| Tocilizumab | 2/23 |
| Rituximab | 2/23 |

All patients from JIA and control group received quality assessment questionnaires SF-36 and functional status HAQ. The results of the evaluation are presented in Table 2.

Table 2. Quality of life in young patients with JIA and control group

|  |  |  |  |
| --- | --- | --- | --- |
| Indexes | Patients with JIA (n=89) | Control group (n=25) | p |
| HAQ | 0.3±0.4 |  |  |
| VAS patient | 34.6±23.3 |  |  |
| VAS doctor | 27.9±24.3 |  |  |
| SF- 36 | | | |
| SF-36 physical indexes | | | |
| **PF** | **74.3± 20.9** | **94.7±8.7**  **0.0002** | |
| **RF** | **64.6±29.9** | **83.8±19.5 0.02** | |
| **BP** | **59.0±24.2** | **84.5±21.6** | **0.0002** |
| GH  56.5±22.6 | | 60.1±17.1 | 0.54 |
| VT | 58.2±19.1 | 59.8±20.0 | 0.77 |
| SF-36 psychological indexes | | | |
| SF | 75.8±21.2  69.2±33.8  69.3±18.6  **46.3±8.7** | 80.5±18.2 | 0.41  0.52 |
| RE | 75.0±26.7 |
| MH | 68.4±18.9 | 0.86 |
| **PCS** | **55.7±6.9** | **0.0001** |
| MCS | 47.0±10.5 | 45.1±11.7 | 0.52 |
| PHQ-9 | 5.8 ±5.5 | 4.3 ±3.1 | 0.12 |

\* Notes: PF - physical functioning; RP - role functioning due to physical condition, BP- pain intensity, GH - general health status, VT - vital activity, SF - social functioning, RE - role function, conditioned by emotional state, MH - mental health, PCS - Physical well-being, PCS - psychological well-being.

|  |  |  |  |
| --- | --- | --- | --- |
| HAQ | 0.3±0.4 | 80.99±18.29  75.99±26.79 | 34.55 |
| VAS patient - 34.6±23.3 | | 32.33 |
| VAS doctor | 27.9±24.3 | 68.99±18.99 | 26.55 |

As can be seen from Table 2, patients with JIA had a worse (p<0.001) physical well-being (46.3±8.7) compared with the control group (55.7±6.9). In them, there was a decrease in the indices corresponding to the physical condition (p<0.001), role functioning due to the physical condition (p=0.02), and the intensity of pain (p<0.001), compared with the control group. However, the indicators responsible for psychological well-being in patients with JIA did not differ from the control group.

In the analysis of functional activity communication for HAQ (Table 3), there was found a strong negative effect on physical functioning (r = -0.56, p<0.001), a role-based functioning due to physical condition (r = -0.33, p <0.001), pain intensity (r = -0.60, p<0.001), general health (r = -0.40, p = 0.01), vital activity (r = -0.46, p <0.001), social functioning (r = -0.48, p<0.001), and mental health (r = -0.42, p<0.001), as well as in the total score for the physical (p<0.001) and psychological (p<0.05) well-being.

Table 3. Communication of functional activity with quality of life.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | PCS | MCS | PF | RF | BP | GH | VT | SF | RE | MH |
| HAQ | -0.59 | -0.25 | -0.56 | -0.32 | -0.60 | -0.40 | -0.46 | -0.48 | -0.08 | -0.42 |
| P | <0.001 | 0.035 | <0.001 | 0.006 | <0.001 | 0.001 | <0.001 | <0.001 | НД | <0.001 |

Figure 1 shows the results of the SF-36 questionnaire for young patients with JIA and those in the control group, where the apparent lower levels of physical health (PCS) (p<0.001), role-based physical functioning are evident) - RF (p<0, 05), pain intensity - BP (p<0.001) and physical functioning - PF (p<0.001) in patients with JIA compared with healthy subjects.

Figure 1. Quality of life in young patients with JIA and healthy individuals according to the SF-36 questionnaire.

\*Notes: \* - statistical significance p<0.001, † - statistical significance p=0.05

# Discussion

### Heading 3

As we expected, QoL in patients with JIA was worse than in the control group. Our findings were confirmed by data published earlier that showed a worse QoL in young people with JIA than in the control group of the corresponding age and sex [9, 16, 17, 18, 19, 20, 21]. However, our results in patients with JIA and healthy individuals are different from the data from Wipff J. et al., where authors analyzed data on patients with JIA at the stage of transmission of patients from child to an adult healthcare services during biologic therapy [22]. The SF-36 score for physical and psychological health was less influenced by the JIA in our sample than in previously published studies. These results were quite unexpected because in Ukraine biological therapy is not available for many patients [16, 18, 19, 20, 22]. There are several possible explanations for these results, including:

* Our patients often received GCs, which reduced the activity of the disease.
* Our sample included not only patients with JIA in the active phase that needed constant observation but also those who were in complete clinical remission and did not require medical therapy.
  + Nested List item 1
  + Nested List item 2
* Our results confirmed that JIA's greatest impact was on "physical functioning" and "pain intensity," which are parts of the physical well-being SF-36 factor. Thus, JIA has a greater impact on physical health than on the mental health of patients, which corresponds to scientific data [16, 18, 19, 20, 23, 24].

There is evidence of a negative relationship between QoL and the duration of the disease by the results of work by Minden K. et al. [25]. Foster et al. also noted this tendency in patients with JIA [16]. However, in our study, we did not detect the effect of the duration of the disease on the QoL indicators, although we observed the negative correlation between functional activity limitation and all components of the QoL according to the SF-36 as established, and in the previous work [1] we have shown that QoL depends on the X-ray definite degree of JIA’s progression .

Since our study showed that physical activity is most strongly affected by pain intensity, treatment with JIA should not be directed solely at the fight against inflammation through the use of NSAIDs. It is advisable to use analgesics and procedures for severe pain, including physiotherapy and/or hypnosis [26].

Patients with JIA may also have a low QoL while in remission. In our study, it was found that 3 out of 33 patients in the remission stage had a low physical well-being. In 5 out of 33 patients - a low level of mental well-being. These data coincide with the results of the study [22], in which 8/38 patients with JIA in the remission stage had a low physical well-being.

Our study has some limitations. First, our study had cross-sectional design study that limited the assessment of the natural course and QoL prognostic factors of the JIA. Second, data on the educational and socio-economic status of patients with JIA and their parents have not been collected. These factors may influence SF-36 results. Previous studies have shown that psychological factors, therapies, geographical origin, and socioeconomic differences can have an effect on pain in the JIA [27, 28]. Third, we did not evaluate the effect of treatment on QoL, especially on biological therapy, although a number of studies have shown that QoL with JIA is improved against the background of biological therapy [29, 30].

Our research also has the strengths:

1. The experimental group consisted of patients with JIA that met the criteria for ILAR in the transition period.
2. The results of evaluation were compared with the control groups comprised of healthy individuals.
3. This is the first study in Ukraine that included biologic therapy as a potential factor affecting QoL in the transition period.

# Conclusion

Juvenile idiopathic arthritis had the greatest influence during the transition from pediatric to adult rheumatological service to a physical functioning and pain intensity on SF-36 physical well-being scale. It indicates a greater effect of the disease on the physical than on the mental health in patients with JIA.

# Another conclusion

Звичаний текст тут.

References

1. Dzhus MB. Psycho-emotional condition of young adults with juvenile idiopathic arthritis. Acta Medica Leopoliensia. 2017; 23 (1-2): 44-51.
2. Hersh A, Scheven E, Yelin E. Adult outcome of childhood-onset rheumatic diseases. Nat Rev Rheumatol. 2011;7(5):290-295. DOI: <https://doi.org/10.1038/nrrheum.2011.38> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/21487383>
3. Scal P, Horvath K, Garwick A. Preparing for adulthood: health care transition counseling for youth with arthritis. Arthritis Rheum. 2009;61(1):52-57. DOI: <https://doi.org/10.1002/art.24088> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/19116976>
4. Ammerlaan JW, Scholtus LW, Bijlsma HJ, Prakken BJ, Kruize AA. An urge for change: transitional care for young adults with juvenile idiopathic arthritis. Patient Educ Couns. 2013;92(1):127–129. DOI: <https://doi.org/10.1016/j.pec.2013.02.006> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/23490174>
5. Wells CK, McMorris BJ, Horvath KJ, Garwick AW, Scal PB. Youth report of healthcare transition counseling and autonomy support from their rheumatologist. Pediatr Rheumatol Online J. 2012;10:36. DOI: <https://doi.org/10.1186/1546-0096-10-36>
6. Shaw KL, Southwood TR, McDonagh JE. User perspectives of transitional care for adolescents with juvenile idiopathic arthritis. Rheumatology. 2004;43(6):770–778. <https://doi.org/10.1093/rheumatology/keh175> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/15039498>
7. Eyckmans L, Hilderson D, Westhovens R, Wouters C, Moons P. What does it mean to grow up with juvenile idiopathic arthritis? A qualitative study on the perspectives of patients. Clin Rheumatol. 2011;30(4):459–465. DOI: <https://doi.org/10.1007/s10067-010-1444-0> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/20383546>
8. Tong A, Jones J, Craig JC, Singh-Grewal D. Children’s experiences of living with juvenile idiopathic arthritis: a thematic synthesis of qualitative studies. Arthritis Care Res (Hoboken). 2012;64(9):1392–1404. DOI: <https://doi.org/10.1002/acr.21695> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/22504867>
9. Packham JC, Hall MA. Long-term follow-up of 246 adults with juvenile idiopathic arthritis: functional outcome. Rheumatology (Oxford). 2002;41(12):1428–1435. DOI: <https://doi.org/10.1093/rheumatology/41.12.1436> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/12468825>
10. Magni-Manzoni S, Ruperto N, Pistorio A, Sala E, Solari N, Palmisani E, Cugno C, Bozzola E, Martini A, Ravelli A. Development and validation of a preliminary definition of minimal disease activity in juvenile idiopathic arthritis. Arthritis Rheum. 2008;59(8):1120–1127. DOI: <https://doi.org/10.1002/art.23916> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/18668599>
11. Haverman L, Grootenhuis MA, Berg JM, Veenendaal M, Dolman KM, Swart JF, Kuijpers TW, Rossum MA. Predictors of health- related quality of life in children and adolescents with juvenile idiopathic arthritis: results from a Web-based survey. Arthritis Care Res (Hoboken). 2012;64(5):694–703. DOI: <https://doi.org/10.1002/acr.21609> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/22238240>
12. Kalyoncu U, Dougados M, Daurès JP, Gossec L. Reporting of patient-reported out- comes in recent trials in rheumatoid arthritis: a systematic literature review. Ann Rheum Dis. 2009;68(2):183–190. DOI: <https://doi.org/10.1136/ard.2007.084848> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/18375533>
13. Bruce B, Fries JF. The Health Assessment Questionnaire (HAQ). Clin Exp Rheumatol. 2005;23(5):14–18. PMID: <https://www.ncbi.nlm.nih.gov/pubmed/16273780>
14. Petty RE, Southwood TR, Manners P, Baum J, Glass DN, Goldenberg J, He X, Maldonado-Cocco J, Orozco-Alcala J, Prieur AM, Suarez-Almazor ME, Woo P. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004;31(2):390–392. PMID: <https://www.ncbi.nlm.nih.gov/pubmed/14760812>
15. Beukelman T, Patkar NM, Saag KG, Tolleson-Rinehart S, Cron RQ, DeWitt EM, Ilowite NT, Kimura Y, Laxer RM, Lovell DJ, Martini A, Rabinovich CE, Ruperto N. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res. 2011;63(4):465–482. DOI: <https://doi.org/10.1002/acr.20460> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/21452260>
16. Foster HE, Marshall N, Myers A, Dunkley P, Griffiths ID. Outcome in adults with juvenile idiopathic arthritis: a quality of life study. Arthritis Rheum. 2003;48(3):767–775. DOI: <https://doi.org/10.1002/art.10863> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/12632431>
17. Ruperto N, Levinson JE, Ravelli A, Shear ES, Link Tague B, Murray K, Martini A, Giannini EH. Long-term health outcomes and quality of life in American and Italian inception cohorts of patients with juvenile rheumatoid arthritis; I; Outcome status. J Rheumatol. 1997;24(5):945–951. PMID: <https://www.ncbi.nlm.nih.gov/pubmed/9150087>
18. Flatø B, Aasland A, Vinje O, Førre O. Outcome and predictive factors in juvenile rheumatoid arthritis and juvenile spondyloarthropathy. J Rheumatol. 1998;25(2):366–375. PMID: <https://www.ncbi.nlm.nih.gov/pubmed/9489836>
19. Peterson LS, Mason T, Nelson AM, O'Fallon WM, Gabriel SE. Psychosocial outcomes and health status of adults who have had juvenile rheumatoid arthritis: a controlled, population-based study. Arthritis Rheum. 1997;40(12):2235–2240. PMID: <https://www.ncbi.nlm.nih.gov/pubmed/9416862>
20. Arkela-Kautiainen M, Haapasaari J, Kautiainen H, Vikkumaa I, Malkia E, Leirisalo-Repo M. Favourable social functioning and health related quality of life of patients with JIA in early adulthood. Ann Rheum Dis. 2005;64(6):875–880. DOI: <https://doi.org/10.1136/ard.2004.026591>
21. Oen K, Malleson PN, Cabral DA, Rosenberg AM, Petty RE, Reed M, Schroeder ML, Cheang M. Early predictors of longterm outcome in patients with juvenile rheumatoid arthritis: subset-specific correlations. J Rheumatol. 2003;30(3):585–593. URL: <http://www.jrheum.org/content/30/3/585.long> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/12610821>
22. Wipff J, Sparsa L, Lohse A, Quartier P, Kahan A, Deslandre CJ. Impact of juvenile idiopathic arthritis on quality of life during transition period at the era of biotherapies. Joint Bone Spine. 2015 <https://doi.org/10.1016/j.jbspin.2015.03.005> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/26231098>
23. Ding T, Hall A, Jacobs K, David J. Psychological functioning of children and adolescents with juvenile idiopathic arthritis is related to physical disability but not to disease status. Rheumatology (Oxford). 2008;47(5): 660–664. DOI: <https://doi.org/10.1093/rheumatology/ken095> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/18356173>
24. LeBovidge JS, Lavigne JV, Donenberg GR, Miller ML. Psychological adjustment of children and adolescents with chronic arthritis: a meta-analytic review. J Pediatr Psychol. 2003;28(1):29–39. DOI: <https://doi.org/10.1093/jpepsy/28.1.29> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/12490628>
25. Minden K, Niewerth M, Listing J, Biedermann T, Bollow M, Schöntube M, Zink A. Long-term outcome in patients with juvenile idiopathic arthritis. Arthritis Rheum. 2002;46(9):2392–2401. DOI: <https://doi.org/10.1002/art.10444> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/12355487>
26. Stinson JN, Luca N, Jibb LA. Assessment and management of pain in juvenile idiopathic arthritis. Pain Res Manag. 2012;17(6):91–396. DOI: <https://doi.org/10.1155/2012/237258> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/23248812>
27. Jordan JM. Effect of race and ethnicity on outcomes in arthritis and rheumatic conditions. Curr Opin Rheumatol. 1999; 11(2):98–103. DOI: <https://doi.org/10.1097/00002281-199903000-00003> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/10319211>
28. Baker TA, Green CR. Intrarace differences among black and white Americans presenting for chronic pain management: the influence of age, physical health, and psychosocial factors. Pain Med. 2005;6(1):29–38. DOI: <https://doi.org/10.1111/j.1526-4637.2005.05014.x> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/15669948>
29. Klotsche J, Minden K, Thon A, Ganser G, Urban A, Horneff G. Improvement in Health-related Quality of Life for children with juvenile idiopathic arthritis after start of treatment with etanercept. Arthritis Care Res (Hoboken). 2014;66(2):253–262. DOI: <https://doi.org/10.1002/acr.22112> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/23983081>
30. Prince FH, Geerdink LM, Borsboom GJ, Twilt M, Rossum MA, Hoppenreijs EP, Cate RT, Koopman-Keemink Y, Santen-Hoeufft M, Raat H, Suijlekom-Smit LW. Major improvement in health-related quality of life during the use of etanercept in patients with previously refractory juvenile idiopathic arthritis. Ann Rheum Dis. 2010; 69(1):138–142. DOI: <https://doi.org/10.1136/ard.2009.111260> PMID: <https://www.ncbi.nlm.nih.gov/pubmed/19581280>

# Bibliography

Frankova, I. A., & Semenoga, P. P. (2014). Second journal article title. *Demo Journal*, 224-255.

Moroz, F. S., & Bezsheiko, V. G. (21 4 2018 г.). Simple journal article: first citation. *Demo Journal*, стр.

# Zotero

1.  Chandler V. Google and suicides: what can we learn about the use of internet to prevent suicides? Public Health. 2018 Jan 1;154:144–50.