Hot Articles

“November | 2019”

Health Science
Abstract

**Introduction:** Intralesional therapies have emerged as effective immune therapies for locally advanced and metastatic melanoma. Talimogene laherparepvec (T-VEC), an oncolytic virus derived from the herpes simplex 1 (HSV-1) virus, is the first and only FDA approved intralesional therapy for recurrent, unresectable cutaneous, subcutaneous or nodal metastases from melanoma.

**Areas covered:** We discuss results from clinical trials of T-VEC including data on safety, biodistribution, and viral shedding, which established the current treatment protocol and basis for FDA approval. Data are presented from early implementation of T-VEC in clinical practice. We explore use of T-VEC in the neoadjuvant setting and in combination with anti CTLA-4 and PD-1 therapies, including available evidence to support a mechanism for the observed synergistic effect.

**Expert opinion:** Intralesional T-VEC is effective for unresectable stage III and IVa melanoma, with early clinical results comparing favorably to response rates from clinical trials. Clinical applications will likely increase as more data become available on its use in the neoadjuvant setting and in combination with other systemic immune therapies. We expect the fields of intralesional therapy and viral oncotherapy to expand as we better understand how to manipulate the tumor microenvironment and host immune response to cancer.
A Critical Review of Qualitative Interview Studies with Alcoholics Anonymous Members

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Substance Use & Misuse

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Abstract

**Background:** Alcoholics Anonymous (AA) is a community-based NGO that supports people with alcohol misuse concerns to achieve and maintain abstinence. Qualitative methods are best suited to investigate individual experiences of recovery in AA, since this typically involves not only abstinence from alcohol but also the global psychological growth of the whole person. Despite this, the growing body of qualitative research exploring individual experiences in AA has yet to be collated. **Objectives:** The aims of this paper were to systematically search for and critically review qualitative interview studies with AA members. **Methods:** A systematic database and citation search identified 21 articles published between 1977 and 2014. Two independent reviewers assessed each research report and extracted data pertaining to the findings and the methodological quality of the studies. **Results:** Major themes across the reviewed articles included ‘rock-bottom’ experiences and powerlessness, and identity and change processes in AA. Findings related to the methodological quality of the papers were both general to qualitative research and more specific to AA. **Conclusions/Importance:** Research in this field has been characterized by a relatively uncritical discovery of AA narratives among AA members and by a lack of methodological rigor, which is likely to perpetuate its negative standing in the context of academia, and therefore in public and political discourse. Overall, findings demonstrated a pressing need for high quality qualitative research on AA.

Database

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Collegian help seeking: the role of self-compassion and self-coldness

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Journal of Mental Health

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Abstract

Background: Researchers have identified a two-factor structure of self-compassion (i.e. self-compassion and self-coldness). To date, no research has examined each of these constructs’ role in collegian professional help-seeking intention.

Aim: The current study sought to assess the role of self-compassion and self-coldness in collegian professional help-seeking intention, accounting for other theoretically and empirically-supported help-seeking constructs.

Method: Participants included 9349 collegians recruited as part of the national 2015–2016 Healthy Minds Study archival dataset. A logistic regression was conducted to examine the unique contributions of self-compassion and self-coldness in predicting professional help-seeking intention, controlling for key help-seeking variables.

Results: A test of the full model against a constant only model was statistically significant, which indicated that the predictors collectively distinguished between collegians who intended to seek help from a professional clinician compared to those who did not. The Wald criterion indicated that both self-compassion and self-coldness were uniquely associated with intention to seek professional help. Self-compassion increased and self-coldness decreased the probability of seeking professional help.

Conclusions: The study highlights the importance of self-compassion and self-coldness in collegian help-seeking intention. These findings can inform specific outreach efforts targeting both self-compassion and self-coldness.
Abstract

Purpose: The present study evaluated biochemical as well as biophysical mechanisms behind the synergistic effects of curcumin and resveratrol during prostate carcinogenesis.

Methods: The rats were segregated into five groups that included normal control, 3,2'-dimethyl-4-aminobiphenyl (DMAB)treated, DMAB + curcumin treated, DMAB + resveratrol-treated and DMAB + curcumin + resveratrol-treated.

Results: The DMAB treatment resulted in a significant increase in the levels of lipid peroxidation (LPO) in DMAB treated rats. Also, significant changes were recorded in the enzyme activities of both drug metabolising enzyme and antioxidant enzymes after DMAB treatment. Further, radiorespirometric studies showed a significant increase in the 14C-glucose turnover as well as 14C-glucose uptake in the prostate slices of DMAB treated rats. Moreover, a significant rise in cell proliferation was confirmed indirectly by enhanced uptake of 3H-thymidine in the prostate slices of DMAB treated rats. Interestingly, combined treatment of curcumin and resveratrol to DMAB treated animals resulted in a significant decrease in lipid peroxidation, 14C glucose uptakes/turndover and 3H-thymidine uptake in the DMAB treated rats. Besides this, curcumin and resveratrol in combination significantly modulated biochemical indices including drug-metabolising enzymes; antioxidant enzymes in DMBA treated rats.

Conclusion: The study, therefore, concludes that the combination of curcumin and resveratrol holds strong modulatory potential against prostate carcinogenesis.
Title: Developing and testing models to predict mortality in the general population
Author: Alexander Goldfarb-Rumyantzev, Robert S. Brown, Ning Dong, Gurprataap S. Sandhu, Parag Vohra & Shiva Gautam
Journal: Informatics for Health and Social Care
Volume: Published online: 01 Nov 2019
Doi: https://doi.org/10.1080/17538157.2019.1656209

Abstract

We have previously proposed an approach using information collected from published reports to generate prediction models. The goal of this project was to validate this technique to develop and test various prediction models. A risk indicator (R) is calculated as a linear combination of the hazard ratios for the following predictors: age, male gender, diabetes, albuminuria, and either CKD, CVD or both. We developed a linear and two exponential expressions to predict the probability of the outcome of 2-year mortality and compared to actual outcome in the target dataset from NHANES. The risk indicator demonstrated good performance with area under ROC curve of 0.84. The linear and two exponential expressions generated similar predictions in the lower categories of risk indicator (R ≤ 6). However, in the groups with higher R value, the linear expression tends to predict lower, and the exponential expressions higher, probabilities than the observed outcome. A Combined model which averaged the linear and logistic expressions was shown to approximate the actual outcome data the best. A simple technique (named Woodpecker™) allows derivation functional prediction models and risk stratification tools from reports of clinical outcome studies and their application to new populations by using only summary statistics of the new population.

Database

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Abstract

Objective: The objective of this study was to evaluate the frequency of genetic lesions in pharmacists and nurses who prepare and/or handle antineoplastic agents and to evaluate whether there are traces of contaminants in the urine of these professionals.

Methods: A total of 59 professionals participated in the study, of which 10 were non-exposed professionals (controls), 25 were pharmacists, and 24 were nurses.

Key findings: There was a significant increase in genetic damage in lymphocytes and cells of the oral mucosa in both pharmacists and nurses. The levels of cyclophosphamide and ifosfamide were also increased in the urine samples from those individuals. Conclusions: These results demonstrate the growing need for genetic biomonitoring and biomonitoring of trace antineoplastic agents in the urine of health professionals who prepare and/or handle antineoplastic agents.
Title: PROTOCOL: Health, social care and technological interventions to improve functional ability of older adults: Evidence and gap map

Author: Vivian Welch, Tracey E. Howe, Sue Marcus, Christine M. Mathew, Ritu Sadana, Morwenna Rogers, Lisa Sheehy, Johan Borg, Kevin Pottie, Joanna Thompson-Coon, Anne Lyddiatt, Elizabeth Kristjansson, Jason W. Nickerson, Peter Walker, Peter Tanuseputro, Beverly Shea, Heidi Sveistrup, Panteha Babelmorad, Wei Zhang

Journal: Campbell Systematic Reviews

Volume: First published: 10 October 2019

Doi: https://doi.org/10.1002/cl2.1054

Abstract

Background: Summarize the rationale and scope of the evidence and gap maps EGM (ER4).

Objectives: State the main objective(s), preferably in a single concise sentence (ER5).

Search Methods: Provide concise details of search strategies (ER6-8).

Selection Criteria: Provide concise details of selection criteria, (ER6-8).

Data Collection and Analysis: Provide concise details of data collection and analyses (ER6-8).

Main Results: Briefly provide a number of included studies, study characteristics, and risk of bias (ER9-11). Identify clusters of evidence and evidence gaps (ER10).

Authors’ Conclusions: Include implications for research (ER12).

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Wiley Online Library
Abstract

Alcohol abuse and alcohol withdrawal syndrome are major problems in the United States. This retrospective chart review assessed efficacy and safety of propofol plus dexmedetomidine used in combination as adjunctive therapy to benzodiazepines compared with either agent used alone in the treatment of severe alcohol withdrawal. Patients admitted to the intensive care unit and experiencing severe alcohol withdrawal between September 1, 2015, and September 30, 2018, were assessed for eligibility. Primary end points were change in the revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar) score and incidence of bradycardia and hypotension. The combination of propofol and dexmedetomidine was associated with a change in CIWA-Ar score of $-10.4$ (95%CI $-13.5$ to $-7.3$) points compared with $-4.7$ (95%CI $-6.6$ to $-2.8$) points with propofol and $-4.4$ (95%CI $-7.4$ to $-1.4$) with dexmedetomidine ($P = .21$). Bradycardia was experienced by 11.1% of patients receiving the combination, 15.4% of patients receiving propofol, and 28.6% of patients receiving dexmedetomidine ($P = .40$). Patients receiving dexmedetomidine experienced hypotension at a rate of 21.4% compared with 22.2% of patients receiving the combination and 38.5% of patients receiving propofol ($P = .08$). Patients in the combination group also had a shorter length of hospital and intensive care unit stay and shorter time to extubation when compared with the propofol and dexmedetomidine groups. Although no statistical significance was found, the combination was associated with better efficacy and safety outcomes than produced by either agent used alone.
Abstract

Nerve damage can lead to movement and sensory dysfunction, with high morbidity and disability rates causing severe burdens on patients, families, and society. DNA methylation is a kind of epigenetics, and a great number of previous studies have demonstrated that DNA methylation plays an important role in the process of nerve regeneration and remodeling. However, compared with the central nervous system, the peripheral nervous system shows stronger recovery after injury, which is related to the complex microenvironment and epigenetic changes occurring at the site of injury. Therefore, what common epigenetic changes between the central and peripheral nervous systems remain to be elucidated. We first screened differential methylation genes after spinal cord injury and sciatic nerve injury using whole-genome bisulfite sequencing and methylated DNA immunoprecipitation sequencing, respectively. Subsequently, a total of 16 genes had the same epigenetic changes after spinal cord injury and sciatic nerve injury. The Gene Ontology analysis and Kyoto Encyclopedia of Genes and Genomes enrichment analysis were performed to identify the critical biological processes and pathways. Furthermore, a protein–protein interaction network analysis indicated that Dnm3, Ntrk3, Smurf1, Dpysl2, Kalrn, Shank1, Dlg2, Arsb, Reln, Bmp5, Numbl, Prickle2, Map6, and Htr7 were the core genes. These outcomes may provide novel insights into the molecular mechanism of the subacute phase of nerve injury. These verified genes can offer potential diagnostic and therapeutic targets for nerve injury.

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Abstract

OBJECTIVE. The purposes of this study were to estimate the blood volume flow of the lower extremities by means of Doppler technique; to establish a quantitative relationship between volume flow and pulsatility index (PI) in both healthy subjects and patients with peripheral artery disease (PAD); and to derive arterial blood flow equations in the lower extremities for more accurate volume flow estimations.

SUBJECTS AND METHODS. Sixty healthy subjects were recruited. Arterial diameter, peak systolic velocity, PI, time-averaged mean velocity, and volume flow of right lower extremity arteries were measured with duplex Doppler ultrasound. Linear regression analysis was used to evaluate the relationship between volume flow and the reciprocal of PI. This quantitative relationship was also used to assess flow changes in 10 patients with PAD before, after, or both before and after percutaneous angioplasty.

RESULTS. Volume flow in the common femoral artery was 434.4 mL/min; superficial femoral artery, 172.5 mL/min; popliteal artery, 92.1 mL/min; dorsalis pedis artery, 11.8 mL/min; and common plantar artery, 12.0 mL/min. Linear relationships between the reciprocal of PI and volume flow were found and expressed as linear blood flow equations. For the patients with PAD, no statistical increase in measured flow in the downstream artery after percutaneous angioplasty was found (p = 0.1), although four arteries had decreased flow. After normalization of flow measurements with PI values, however, statistical increases were observed between percentage increment (p < 0.001) calculations.

CONCLUSION. When real-time PI values are factored into blood volume flow calculations in the evaluation of lower extremity arteries, discrepancies in flow measurements can be resolved, resulting in more accurate and stable measurements of clinical and diagnostic significance.

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